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SCIENCE

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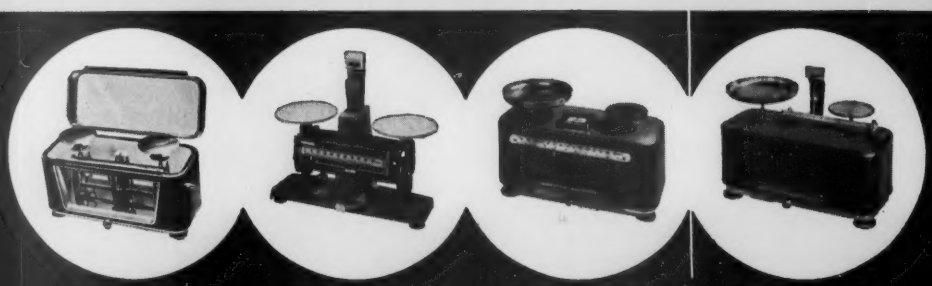

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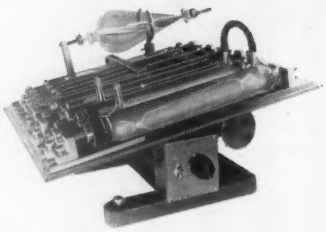

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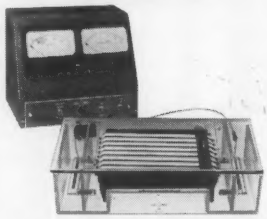

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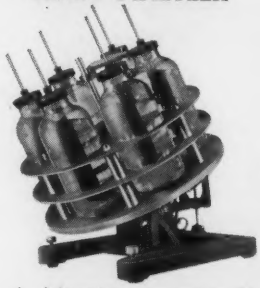

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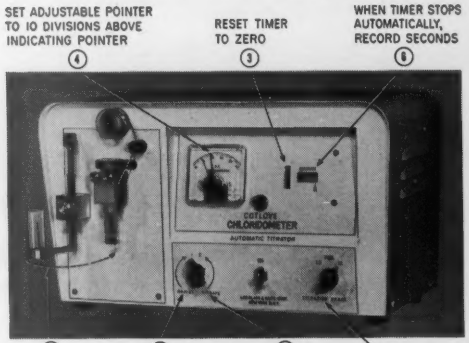

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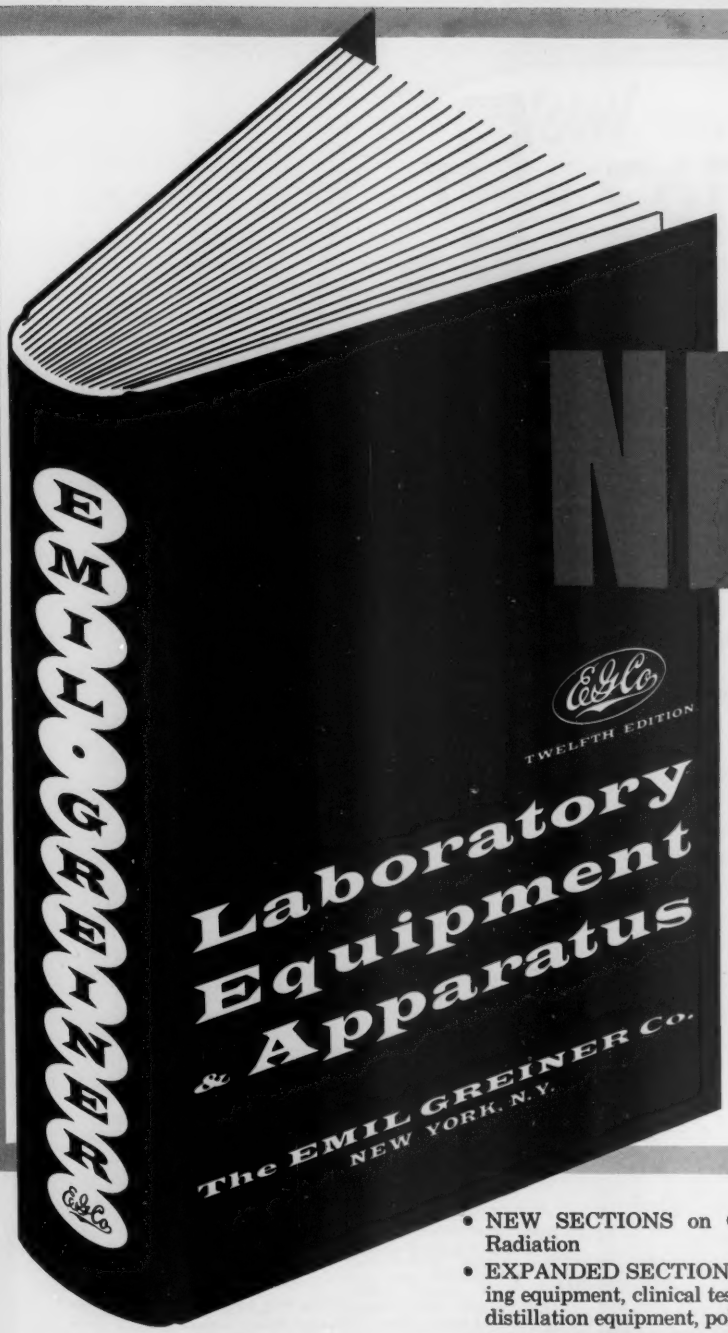

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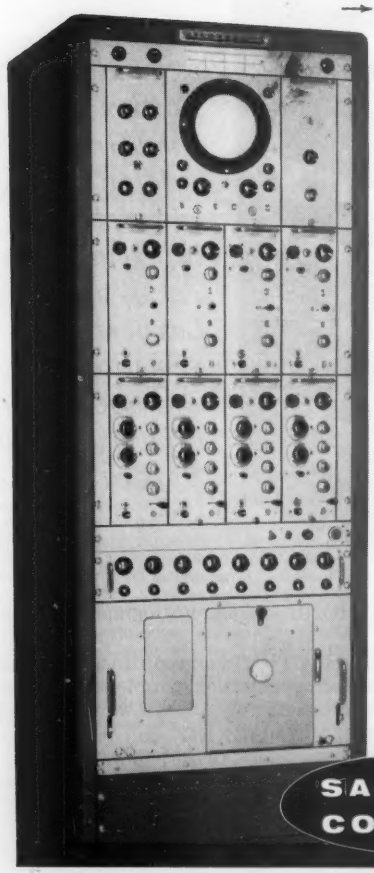

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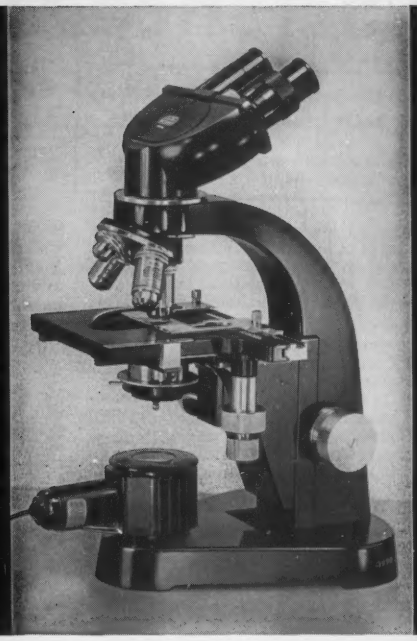

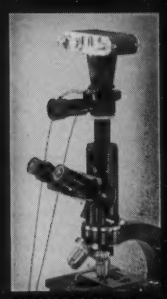

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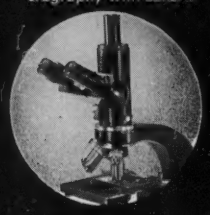

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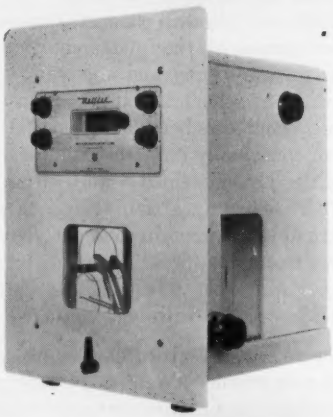

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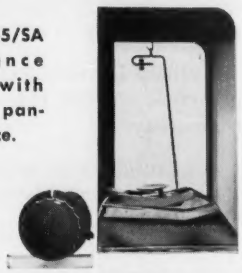

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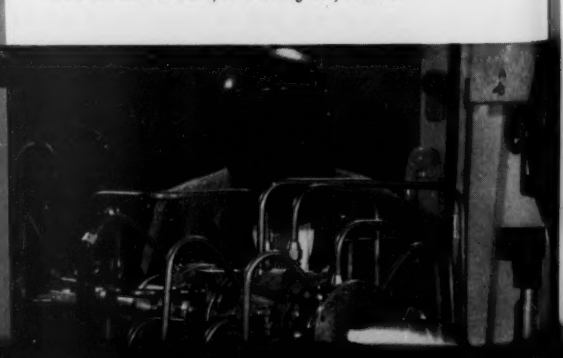

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To Be Continued

With the experts having agreed at Geneva on the feasibility of monitoring a suspension of nuclear test explosions, the problem of suspension now rests in the hands of the people who conduct political negotiations. The West has proposed and the East has accepted a plan to begin talks on 31 October about such matters as where the 180-odd control posts are to be located and who is to man them. On the same date the United States and Britain will begin a one-year suspension of nuclear test explosions which will be renewed on a year-to-year basis, depending upon the success of the talks, upon progress in other phases of arms control, and upon Russia's not resuming her own test explosions. But besides its bearing on the suspension of nuclear tests, the Geneva conference may also have other results. The conference may provide a pattern for reaching agreement on other aspects of international arms control, the pattern being to explore questions of scientific possibility before turning to questions of political reality.

One good candidate for some future application of the Geneva pattern is the problem of safeguarding nations against surprise attacks. With the increasing shift from manned bombers to space-missiles, the danger posed by the possibility of a surprise attack includes not only the possibility of one nation launching an attack upon a second, but of a fatal false alarm in the second nation's defense warning system. Some ghastly compounding of mechanical defect and human mistake may mean that a false alarm is not identified as false in sufficient time to prevent the second nation from launching its counteroffensive. The problem of surprise attacks is a good candidate for negotiations because, like the suspension of nuclear test explosions, an international system to safeguard nations against surprise attack has common advantages for both East and West.

Although in the Geneva pattern scientific talks precede political talks, still the decision to seek scientific talks is itself a political decision, and the success of future talks may well depend upon the kind of priority assigned to them. The question of priority arises because the requirements of a scientific conference may well work against the other requirements of this country's welfare. In the matter of security, for example, getting down to details in considering the feasibility of a detection network may also mean getting down to details that have been classified secret by one department in the Government or another. The problem is how much secret information our representatives at a conference should be permitted to reveal if they deem it necessary. It would be interesting to know in this connection what kind of authority our participants in the Geneva conference had to disclose technical points that had previously been classified.

Most scientists, like most other people in this country, are something less than happy that their efforts for national defense seem necessarily to result in weapons of ever greater destructive power. In seeking to make us ever more secure, scientists find themselves creating the possibility of ever greater catastrophe. Consequently, many scientists wonder if there is not some action that they as scientists can take to neutralize the threat to civilization that their own achievements are posing. Part of the answer may lie in the pattern set by the Geneva conference. Scientists can develop the different instruments of inspection appropriate to the various aspects of arms control. If the art of war has become dependent in good part upon the efforts of scientists, then so has the art of making peace.—J.T.

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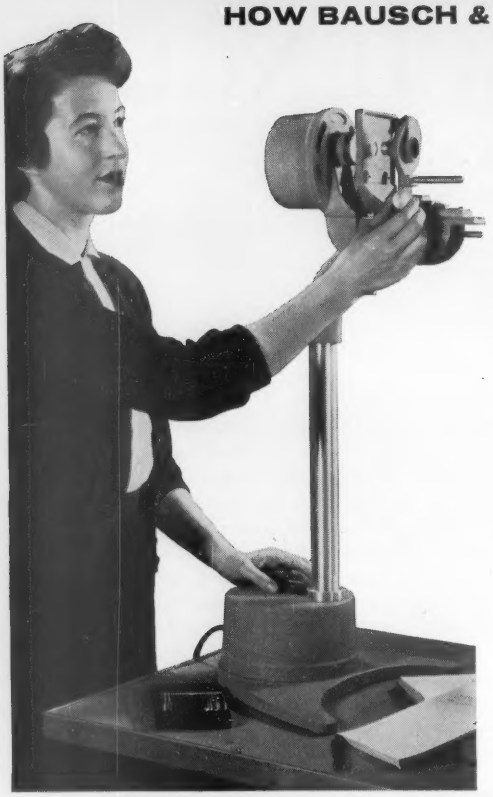

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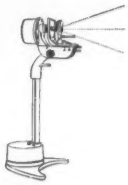

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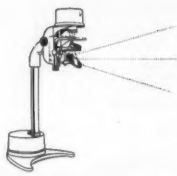

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12 September 1958, Volume 128, Number 3324 SCIENCE

CURRENT PROBLEMS IN RESEARCH

Growth and Properties of "Whiskers"

Further research is needed to show why crystal filaments are many times as strong as large crystals.

S. S. Brenner

The one outstanding characteristic of most single crystals is their weakness. Refining earlier estimates, Mackenzie (*1*) arrived at the conclusion that the shear strength of a crystal should at least be 3 percent of its shear modulus (μ). In practice, crystals usually deform plastically when stressed less than 10^{-4} μ.

In 1952 Galt and Herring (*2*) demonstrated that at least some crystals possess the strength predicted by theory. These crystals were tiny filaments of tin (Fig. 1), about 2 microns in diameter and a few millimeters in length, that had been discovered several years earlier (*3*) and descriptively termed "whiskers." Although filamentary crystals have been the subject of numerous philosophical and scientific discussions during the last 200 years, this was the first time that it was recognized that they possess unusual properties. A large number of publications have appeared since 1952 dealing both with the properties and growth of whiskers. The results of most of these investigations have been interpreted in terms of the dislocation theory, which has been so widely applied in metallurgy and solid-state physics. Since whisker research has already made a significant contribution in the field of crystal growth and strength of solids, and since whiskers will undoubtedly be of continuing interest for a number of years, it is felt that a review of our knowledge of their growth and properties is appropriate at this time. Hardy (*4*) has described extensively the early work concerned with the filamentary growth of crystals, and hence greater emphasis will be placed in the following pages on the more recent work.

The author is on the staff of the metallurgy and ceramics research department of the General Electric Research Laboratory, Schenectady, N.Y.

Growth of Whiskers

Most of the early discussions on the filamentary habit of crystal growth were concerned with the naturally occurring growth of silver and copper filaments (*Haarsilber* and *Haarkupfer*) on silver and copper ores containing sulfur. These filaments, which sometimes are as long as 15 centimeters, were at one time considered to represent a transition from vegetable to mineral. During the latter part of the 18th century it was demonstrated that they can be produced synthetically by reducing or oxidizing silver and copper sulfide. The experimental results and theoretical interpretations of the growth of these filaments during the last 200 years have been reviewed by Hardy (*4*). The latest interpretation of their growth is that due to Kohlschütter (*5*) and Wagner (*6*), who postulated that the growth of the silver whiskers is caused by the difficulty of nucleating silver particles in silver sulfide when the sulfur is removed. The silver ions and electrons migrate freely in the Ag_2S until they meet a silver nucleus on which they condense. If this nucleus is on the surface, it can be pushed out into the form of a whisker as reduced silver is added at its base.

Several other techniques of whisker growth have been discovered or developed in recent times. Generally, the driving force for the growth of the crystals has either been a decrease in internal or applied stress (recrystallization process) or a decrease in supersaturation (condensation, precipitation, electrodeposition, and so on).

Stress-Induced Whisker Growth

The tin whiskers tested by Galt and Herring were found to grow spontaneously from tin-plated steel at a rate of about 10^{-8} centimeters per second. Compton, Mendizza, and Arnold have made an extensive study of their growth (*7*). By applying pressure to the electroplated coating, Fisher, Darken, and Carrol (*8*) were able to accelerate the growth rate as much as 10,000 times. The growth rate is proportional to the applied pressure; this indicates that the driving force for the growth is the relaxation of the strain within the metal. Franks (*9*) has postulated that whiskers will develop on the free surface of any compressed or internally strained metal if general extrusion is inhibited and if the temperature is sufficiently high for diffusion to be reasonably rapid.

Several mechanisms for the growth of whiskers from the solid phase have been postulated (*9–11*). They all essentially involve the motion of dislocation loops out of the substrate. The initial loop, breaking through the surface, leaves a closed step 1 atomic unit high on the surface, and each successive loop increases the step height by one more atomic unit. The mechanisms differ in the details of the generation of the loops and their motion towards the surface.

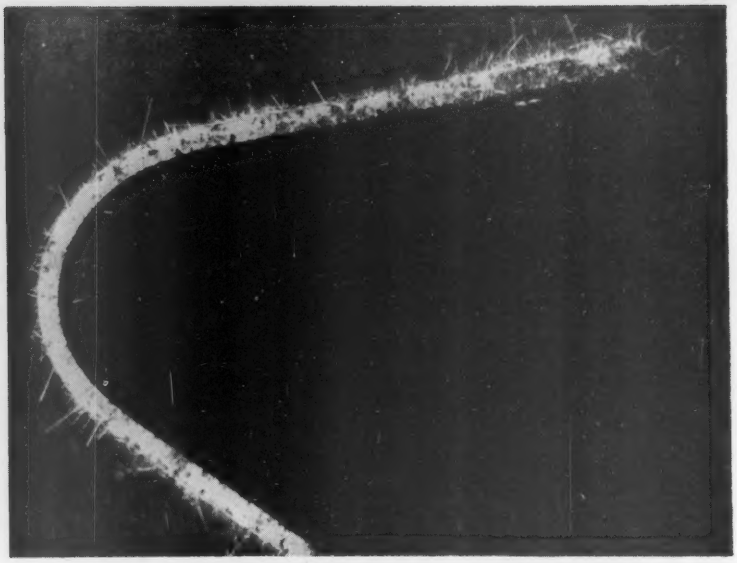


Fig. 1. Whiskers on tin-plated steel. [Compton, Mendizza, and Arnold]

However, they all imply that the whiskers, after growth, either contain no dislocations or at least only a single axial one.

Growth from a Supersaturated Medium; Vapor Deposition

Crystal growth from a supersaturated medium, especially a vapor, has frequently been investigated, both theoretically and experimentally (*12, 13*). It has been recognized that at small supersaturations a molecule or atom from the vapor phase can condense only at a ledge or step on the surfaces of the growing crystal. The classical theory of crystal growth considers a crystal to be structurally perfect and assumes that each time a step on the crystal sweeps over the surface, a new one has to be nucleated on the freshly completed crystal layer (Fig. 2). Since the creation of a step on the surface increases the surface energy of the crystal, a critical supersaturation is required for continued growth. In practice, however, it was found (*13*) that crystals grow at supersaturations which are immeasurably small. Frank, therefore, concluded (*14*) that real crystals are not perfect but contain screw dislocations (Fig. 3) which developed during the early stages of their growth and which provide the crystals with permanent growth steps. As material condenses, the step due to the dislocation winds itself into the form of a spiral because of the greater angular velocity of the step near its emergence. The observation of growth spirals on numerous crystals (*15*) (Fig. 4) provided evidence that Frank's dislocation mechanism of crystal growth is applicable in many cases.

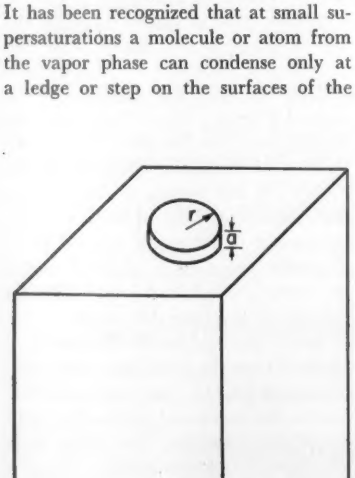


Fig. 2. Nucleation of new crystal layer. Surface energy of crystal increases by $2\pi r a \gamma$ where γ = surface energy.

Volmer and Esterman (*16*) in 1925 found that under certain conditions crystals can grow faster in some directions than in others. They observed that sometimes mercury condenses in the form of thin platelets, with growth occurring many times faster at the crystal edges than at the basal faces. Sears (*17*) extended the work of Volmer and Esterman and found not only platelets but also whiskers. He reported that the shape of the condensed crystals depends on the supersaturation, with three-dimensional massive crystals growing at the highest supersaturations and one-dimensional whiskers at the lowest.

Applying Frank's dislocation theory of crystal growth, Sears (*18*) postulated that the anisotropic growth rate of mercury crystals is due to the absence of dislocations in certain crystal directions. With respect to the whisker habit he proposed that the crystal contains a single dislocation along the center of the crystal, with the lateral crystal surfaces bounded by surfaces which are atomically smooth. The criterion for whisker growth according to this hypothesis is that (i) the whisker embryo contains screw dislocations parallel to only one crystal direction and (ii) during growth the supersaturation of the vapor is less than that required for the nucleation of crystal layers on the lateral surfaces of the crystal. Sears (*19*) has demonstrated that the second requirement is met for the growth of mercury, silver, zinc, cadmium, and cadmium sulfide whiskers from their pure vapor. The first criterion—that the screw dislocations in whiskers, if there are any, are oriented parallel to the whisker axis—has as yet not been demonstrated.

Whisker Growth by Reduction of Halides

A large number of metals can be grown in the form of whiskers by the reduction of halides at elevated temperatures (*5, 20–22*). The method is simple and reproducible. A boat is filled with the halide—for instance, ferrous bromide—and is pushed into a hot furnace through which hydrogen is flowing. During the period of a few hours, filaments, some several centimeters long

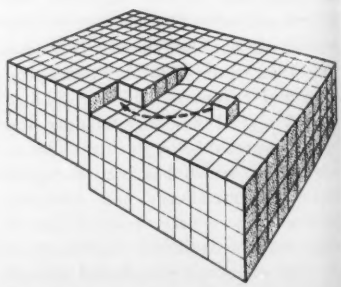


Fig. 3. Screw dislocation intersecting crystal surface, providing crystal with a permanent growth step.

and 1 to 500 microns thick, grow on the sides of the boat. Figure 5 shows some iron whiskers grown by this method.

There are two different mechanisms of growth of these whiskers. Some of the whiskers, notably silver obtained from AgCl, grow at their base (*22*), and hence a mechanism such as that proposed by Wagner and Kohlschütter for the growth of whiskers from sulfides must apply here. In contrast, copper and iron whiskers grow at their tip, and a vapor transport mechanism is most probable. However, experimental results (*22*) and thermodynamic considerations (*23*) indicate that growth does not occur by the direct condensation of metal vapor, and it is most likely that the halide molecules are adsorbed on the growing whiskers and preferentially reduced at the tip. At present the reason for the greater rate of reduction at the tip is not clear. Sears (*24*), extending his whisker growth hypothesis, suggested that these whiskers also contain only axial dislocations. If this is the case, the preferential reduction at the tip may be due to the catalytic reduction of the halide at the step associated with the dislocation. Price, Vermilyea, and Webb (*25*) have suggested for the electrolytic growth of whiskers a mechanism which does not rely on any particular dislocation arrangement and which may be applicable to other methods of whisker growth. They propose that while the lateral surfaces of the whiskers become covered with adsorbed impurities and thus become poisoned, the tip may remain clean because of its rapid rate of advancement.

It is well known that adsorbates have an important influence on crystal growth and crystal habit, and undoubtedly impurity adsorption plays a significant role in whisker growth.

Growth of Whiskers by Precipitation

The precipitation of salts in needle-shaped crystals is not uncommon. The *Handbook of Chemistry and Physics* gives many examples of such crystals, both organic and inorganic. In most cases there probably is no real distinction between whiskers and needles except one of size. With whiskers we usually associate diameters of less than 25 microns. Many of the needle crystals go through a whisker stage during the early part of their growth. This was clearly illustrated by Gordon (*26*) for the precipitation of $MgSO_4 \cdot 7H_2O$, $NiSO_4 \cdot 7H_2O$, quinone, resorcinol, and so on. The precipitated crystal is at first in the form of a fine whisker, which thickens as it weaves through the solution.

The growth of alkali-halide whiskers from aqueous solutions has received particular attention (*27–29*). The solutions are supersaturated either by slowly evaporating the water or by changing the temperature. An interesting method shown in Fig. 6 is that attributable to Amelinckx (*29*). A cellophane bag filled with the alkali halide solution is held suspended for a day or two. During this time the solution permeates the cellophane and, as the water evaporates, leaves a crop of whiskers and other crystals on the outside of the bag.

Dislocation mechanisms have also been applied to the growth of whiskers by precipitation. Sears (*30*) has proposed with respect to the growth of $NaClO_3$ whiskers that the solution migrates along the sides of the whiskers by hydrodynamic flow and the solute is precipitated at the dislocation emerging from the tip. Amelinckx reports that whisker growth on cellophane occurs through the addition of material at the base and proposes that the rate of growth depends on how fast the solution can feed the capillary layer separating the cellophane and the whisker base.

The role of impurities in the growth of whiskers has been found to be signifi-

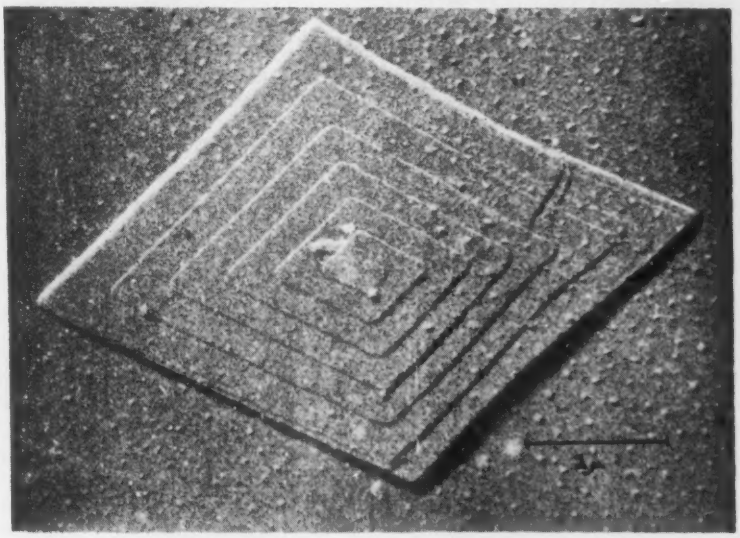
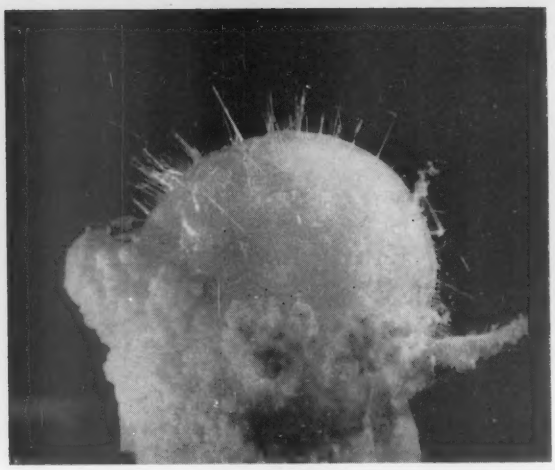


Fig. 4. Growth spiral on paraffin $n - C_{36}H_{74}$. [Verma]

Fig. 5. Iron whiskers grown at 710°C by the hydrogen reduction of ferrous bromide. (About × 5.6)



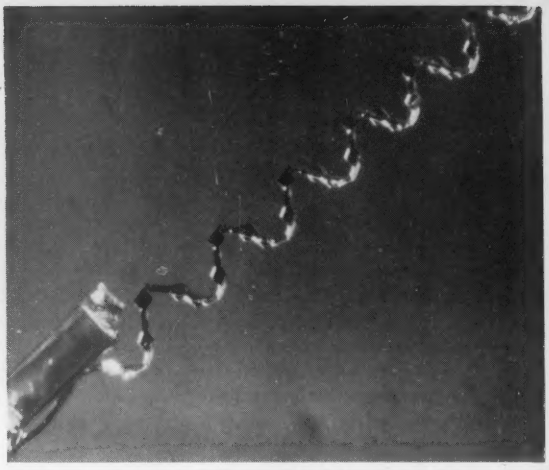


Fig. 6 (Left). Growth of NaCl whiskers on cellophane bag. (About × 1.5). Fig. 7 (Right). Helical copper whisker.

cant. Addition of polyvinyl alcohol or sucrose (*31*) increases the number and length of NaCl whiskers, while addition of a few parts per million of iron salts influences the growth of LiF whiskers (*32*).

Shape, Orientation, and Purity of Whiskers

While most of the whiskers are straight, an amazing variety of shapes frequently occurs in the same batch. Polygonal spirals (*33*), kinks (*34*), twists (*21*), helices (*21*), and many other shapes have frequently been observed. Of considerable interest are the helical whiskers, an example of which is shown in Fig. 7. Little effort has been made to determine the mechanism of growth of these complex shapes. Twinning (*33*) has been associated with some of the kinks in tin whiskers, while Amelinckx *et al.* (*11*) proposed that the kinks reflect the shape of the dislocation network below the surface of the substrate. Sears (*30*) has associated the low-angle bends in $NaClO_3$ with impurity precipitation. Webb and Forgeng (*35*) and Amelinckx (*36*) have suggested that the shape of the helical whisker is due to a precession of the axial growth dislocation. However, since it has not been firmly established that a single axial dislocation is responsible for the growth of even the simplest whiskers, it is somewhat premature to discuss its possible precession.

While many whiskers have simple polygonal or round cross sections (*37*), others are complex in shape. Star-shaped (*38*) and hollow (*35*) cross sections have been reported. An outstanding feature of many whiskers, especially of those that are strong, is the optical perfection of their surfaces. The surfaces of some are smooth at magnifications as high as 40,000.

Most whiskers, including those which are kinked (*39*) and helical (*22*), are single crystals. The axis of the whisker is frequently parallel to a major crystallographic direction. Some whiskers, such as silver from silver sulfide, are polycrystalline with a preferred orientation (*40*).

The purity of whiskers is not exceptionally high. The average impurity content as determined by chemical analyses is about 3×10^{-5} for copper whiskers grown from CuI and 10^{-4} for iron whiskers grown from $FeBr_2$. The lowest residual resistivity measurements obtained thus far indicate about 10^{-4} impurities for zinc (*41*) and copper (*42*).

Mechanical Behavior of Whiskers

The strengths of a large number of whiskers prepared by a variety of methods have been measured, either by means of bend tests or tensile tests. The maximum values are summarized in Table 1. In all cases the maximum elastic strain at the yield point was at least 0.01. In comparison, annealed single crystals usually yield at elastic strains of less than 10^{-4}. The ultimate tensile strengths

Table 1. Strength of whiskers.

Material	Max. elastic strain (%)	Method of testing	Method of growth	Reference
Fe	4.9	Tension	Halide reduction	(*43*)
Cu	2.8	Tension	Halide reduction	(*43*)
Ag	4.0	Tension	Halide reduction	(*43*)
Ni	1.8	Tension	Halide reduction	(*43*)
Si	2.0	Tension	Halide reduction	(*44, 65*)
Zn	2.0	Tension	Vapor condensation	(*66*)
NaCl	2.6	Tension	Precipitation	(*27*)
SiO_2	5.2	Tension	Vapor condensation	(*47*)
Al_2O_3	3.0	Tension	Vapor condensation	(*47*)
MoO_2	1.0	Tension	Vapor condensation	(*47*)
C	2.0	Tension	Vapor condensation	(*67*)
Sn	2 to 3	Bending	Growth from solid	(*2*)
Ge	1.8	Bending	Halide reduction	(*44*)
ZnO	1.5	Bending		(*44*)
ZnS	1.5	Bending	Vapor condensation	(*68*)
LiF	3	Bending	Cleavage	(*69*)
$MgSO_4 \cdot 7H_2O$, hydroquinone, etc.	> 2		Precipitation	(*26*)

of bulk materials compare more favorably with the strength of whiskers, but a work-hardened metal is in a "metastable" condition while the whiskers are annealed.

Not every whisker of a particular substance is as strong as indicated in the table. Efficiency in producing strong whiskers differs with the material and the method of growth. For instance, the value for NaCl given in the table is the highest from about 100 tests, while that for iron is the highest value obtained from about 75 tests. There appears to be some effect of growth conditions on efficiency in producing strong whiskers. Whiskers grown by precipitation from solution or the reduction of halides show a much larger scatter in strength than the whiskers grown under "cleaner" conditions, such as deposition in vacuum or inert atmosphere. Deliberate additions of impurities to solutions have significantly altered the maximum value and scatter of NaCl whiskers (*31*). In spite of the large scatter in strength there is a trend towards lower strengths as the diameter of the precipitation whiskers (*27*) and halide reduction whiskers (*43*) increases (Fig. 8). When the diameters become larger than 25 microns, the strengths approach those of bulk crystals.

The results on strength versus diameter suggest that the whiskers contain weak points which are distributed either on the surface or in the interior of the crystals. As the size of the whisker increases, the number and perhaps degree of weakness of the weak spots may increase, thus giving rise to the decrease in strength. Such weak points are undoubtedly common to all crystals but, in bulk crystals, are overshadowed by other defects which activate plastic deformation at lower stresses.

The number of weak points of a given degree of weakness is small. If a whisker is fractured several times and one of the remaining halves is tested each time, the final strength is often considerably higher than the initial (*43*). For instance, the strength of a copper whisker 4.3 millimeters long increased tenfold when the whisker was successively fractured three times. The final test section was 2.6 millimeters long.

Yielding of Whiskers

When the elastic limit of the whisker is exceeded, either fracture occurs or plastic deformation is nucleated in a localized region. When the elastic limit is exceeded in a whisker strained by bending the whisker kinks; if the kinked whisker is now annealed at a high temperature, it frequently unkinks and recovers its original shape (*27, 44, 45*). In a tensile test the localized plastic region is usually recognizable by the presence of slip line. When a small force is applied, the slipped region travels along the whisker, eventually reaching the extremities of the crystal. Many of the whiskers, including NaCl and LiF, deform plastically as much as 35 percent or more. The flow stress of the stronger whiskers is usually only a small fraction of the yield stress (Fig. 9). Ratios of yield stress to flow stress as high as 90 to 1 (*46*) have been measured. It is of interest to observe that once defects are introduced by means of plastic deformation, the whiskers behave more nearly like bulk crystals. Recovery of the initial high yield stress by annealing at moderate temperatures (*47*) has not been observed except in silicon whiskers (*44*), where the yield stress was partially recovered.

Strength and Perfection

Although whiskers have exhibited the potential strength of perfect crystals, it has not been established whether they are structurally perfect. Structural perfection implies here only the absence of extended defects—in particular, dislocations—and does not include point defects such as vacancies, interstitial atoms, impurities, and electronic defects.

Annealed bulk crystals normally contain from 10^4 to 10^8 dislocations per square centimeter (*48*). These dislocations interact with each other and arrange themselves into networks and boundaries. A crystal deforms plastically by the motion of dislocations, an elongation of about 2×10^{-8} centimeter occurring each time a dislocation leaves the crystal. To account for the large total deformation during plastic flow it has been necessary to postulate that new dislocations are constantly created within the crystal. One dislocation source postulated by Frank and Reed (*49*) supposes that a dislocation segment pinned at two ends repeatedly gives off dislocation loops in somewhat the manner that soap bubbles are formed from a soap-filled loop. The pressure, or stress, required to operate the source is inversely proportional to the length of the pinned dislocation segment. Yield stress data indicate that dislocation sources operating at the yield point of massive crystals must be of the order of 3 to 30 microns in length. Mott (*50*) has suggested that the dislocation sources correspond to the links of a three-dimensional dislocation network. If the width of a crystal is now reduced to less than the average length of these links, it becomes unlikely that it will encompass a dislocation network, and hence the probability of the crystal containing dislocation sources is small.

This leads us to the question of whether whiskers are strong simply because they are small or whether high strength is peculiar to whiskers. Sears's whisker-growth theory assumed a single axial dislocation, which implied high strength since the single dislocation is unlikely to provide the crystal with a dislocation source. There is indirect evidence that Al_2O_3 (*35*) whiskers and Hg

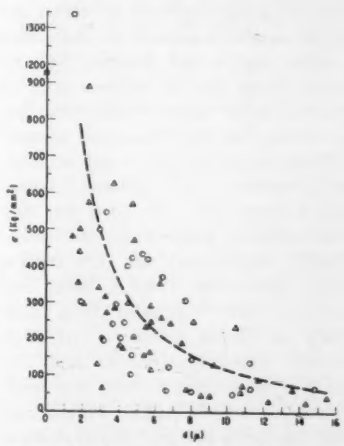


Fig. 8. The strength of iron whiskers as a function of size.

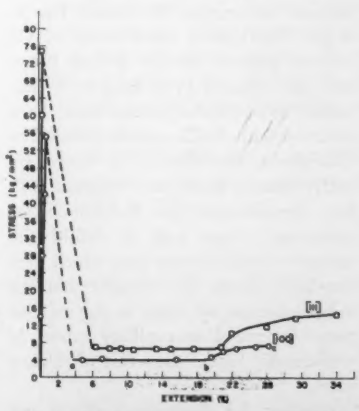


Fig. 9. Stress-strain curve of copper whiskers. After yielding, whiskers deform plastically (*a* to *c*) at much lower stresses.

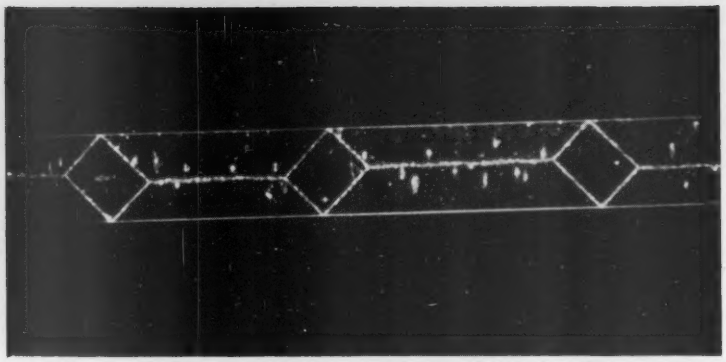


Fig. 10. Domain walls in iron whisker decorated by the Bitter method. (×20) [Graham and DeBlois]

whiskers (*51*) may contain only single axial dislocations. On the other hand, there is no evidence for single dislocations in Fe, Cu, Ni, Zn, and Mn (*52*). Gorsuch (*53*) concluded from his x-ray diffraction experiments that iron whiskers have a high degree of perfection, but he was unable to estimate the dislocation content. Smith and Randle (*54*) recently found that tin whiskers 2 to 11 microns in diameter contain some imperfections but fewer than bulk crystals.

From the growth forms and mechanical behavior of zinc whiskers, Coleman and Cabrera (*55*) concluded that zinc and cadmium whiskers are not exceptionally perfect and that they contain many dislocations. Pearson, Read, and Feldman (*44*) concluded from their work on silicon whiskers that high strength does not necessarily imply absence of dislocations. It must be remembered, however, that silicon is brittle and that fracture is not preceded by dislocation motion at temperatures below 600°C.

There is evidence that size per se can increase the strength of crystals. For instance, the critical shear stress of Cd crystals increases 14-fold if their diameters are reduced by etching to 25 microns (*56*). Smaller effects have been observed with NaCl crystals reduced to 200-micron diameter (*57*). More recently Pearson, Read, and Feldman (*44*) have demonstrated that the strength of 50-micron silicon rods is sixfold the strength of bulk crystals from which they were cut. Taylor (*58*) reports that the tensile strength of wires in the micron range (prepared in capillary tubes) is considerably higher than that of thicker wires.

Whether the dimensional effects are responsible for the total increase in the strength of whiskers can at present not be ascertained from the experimental results. To reach a more definite conclusion it would be desirable to direct research along two avenues: (i) to determine the dislocation content of strong whiskers by some direct means, and (ii) to prepare crystals comparable in size to whiskers from crystals of known perfection. The latter approach presents the difficulty of producing surfaces equivalent to those of whiskers. Indirect evidence has shown that surface imperfections can lower the strength of whiskers considerably (*43*).

Significance of Whisker Research

The greatest significance of whisker research is that it has demonstrated that crystals of strength equal to the strength predicted by theory can be obtained. Gaining an understanding of the cause of their strength will increase our knowledge concerning the mechanical behavior of solids. In addition, an understanding of the mechanism of their growth will be of considerable importance in the field of crystal growth.

Aside from these considerations, whiskers have proven useful in studies that require crystals with (i) high elastic strength, (ii) surface perfection, or (iii) small dimensions. For instance, it has been possible to observe large deviations from Hooke's law in iron and zinc. Seeger (*59*) has made use of the data on iron to compute second-order elastic coefficients.

Important contributions have been made in the field of magnetism through the use of iron whiskers. The whiskers have a simple orientation and lend themselves readily to the study of domain wall patterns (*60*) (Fig. 10), from which a number of interesting observations have been made. Because of their surface perfection, coercive forces of close to the estimated theoretical limit of 530 oersteds have been obtained (*61*). In bulk crystals, domain wall nucleation occurs at much lower fields at imperfections on the surface. By applying these high coercive forces, domain wall velocities in excess of 50 kilometers per second were measured, whereas earlier measurements had been limited to velocities of less than 0.3 kilometers per second.

Whiskers have become useful in studies of corrosion and electrolysis. Green and Woolf (*62*) report a decreased rate of corrosion of silver whiskers in 8*N* nitric acid, while the rate of oxidation of iron whiskers at 500°C (*42*) is sometimes only 2 percent of the corrosion rate of polycrystalline iron. Vermilyea (*63*) found that the overvoltage for deposition on thin copper whiskers is sometimes ten times larger than the overvoltage that is required for deposition on bulk copper.

Whiskers are useful in studies where size effects are important, such as electrical resistivity at low temperatures. Lutes (*64*), using tin whiskers, showed that size has an important effect on superconductivity.

Conclusion

Crystals in the form of thin filaments or whiskers have strengths which are sometimes between 100 and 1000 times greater than those of large crystals. At present it is not known whether their strength is due to their small size, their surface perfection, a unique structural perfection, or a combination of these factors. Small crystals prepared from large imperfect crystals have shown an increase in strength, but whether strengths equivalent to the strength of whiskers can be obtained by decreasing the size of such crystals still further is at present uncertain. A knowledge of the cause of whisker strength is of importance both for technological and scientific reasons. Most mechanisms of whisker growth that have been proposed assume a unique dislocation density and orientation in the whiskers. If this assumption is invalid, the present hypothesis will have to be modified. Technologically it is of importance to know the cause of the whisker strength, for only if the strength is due to a unique perfection of either the surface or the interior is there some hope of realizing the high strengths in bulk crystals.

In the meantime, whiskers are proving to be useful tools in many areas of research. As the methods of their growth become more widely known and experience is gained in their handling, their use will become increasingly more widespread.

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Biological Sulfate Activation and Transfer

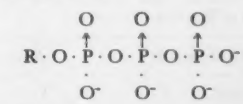
Studies on a mechanism of group activation and its role in biosynthesis are described.

Fritz Lipmann

Sulfate is bound, mostly in ester linkage, in a fairly large variety of compounds present rather commonly in living organisms. Of most importance among these compounds are the sulfated mucopolysaccharides, such as chondroitin sulfuric acid, the ground substance of cartilage, and the similar mucoitin-sulfuric acid in mucosous tissues. Heparin belongs in this group; it is outstanding for its high sulfate, partially bound here to the amino group of the glucosamine moiety. Furthermore, a sulfurylated cerebroside is present in the brain and other tissues. On the other hand, conjugation with sulfate is a means of phenol detoxication in the animal body. This sulfate conjugation of the phenols, mainly in liver and the intestine, has been used for many years for the study of the mechanism of sulfate transfer.

With such a large number of metabolically-formed sulfurylated substances, it appeared likely that there was a common metabolic carrier for activated sulfate which would serve as general sulfate donor in the enzymatic set-up of cells. This was all the more indicated when DeMeio (*1*), who pioneered in the field of sulfate activation, demonstrated that, in cell-free systems, ATP (*2*) could serve as the source of energy for sulfate activation. The kind of mechanism that occurs in sulfate activation was further clarified by Bernstein and McGilvery (*3*). All this work with the liver system indicated strongly that conjugation with phenol was a two-phasic process, the activation of sulfate being the primary, the transfer to phenol being a secondary and separate, step.

Since, therefore, in the process of activation the energy of a phosphoanhydride link of ATP



(1)

apparently was transmitted to the sulfate, it seemed likely that the formation

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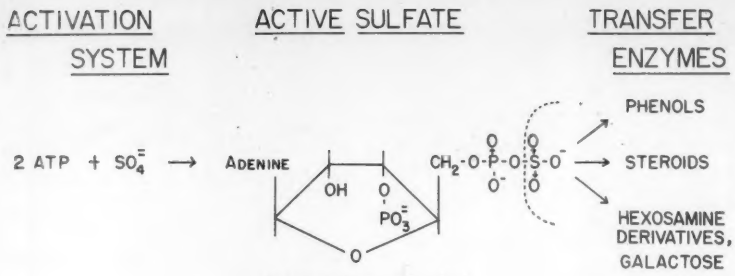
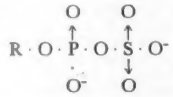


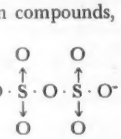
Fig. 1. Sulfate activation.

of a *mixed* anhydride between sulfate and phosphate,



(2)

might represent this process of activation. However, no information about the chemistry of such a mixed anhydride was found in the literature. Pyrosulfates are well-known compounds,



(3)

but they are very sensitive to water and are apparently about as unstable as organic acid anhydrides. For all these reasons, sulfate activation presented a rather special problem in group activation which seemed most attractive to me, and my co-workers and I decided, some three years ago, to try our hand at clearing up the chemistry of this intriguing reaction.

It will be helpful to start with the scheme in Fig. 1, which gives the essentials of the activation-transfer process as we were able to develop it. What I want to stress particularly is the strict separation between the activation process and the transfer reactions. The active sulfate is formed, as we now know and will explain in detail later, by a reaction between sulfate and two ATP's (*4, 5*), as a result of which adenosine-3′-phosphate-5′-phosphosulfate is formed. This appears to be the general sulfate donor in biological reactions, which, as suspected, carries sulfate in the form of a mixed anhydride. We have found this to be a sulfate donor in all cases studied so far —that is, in chondroitin sulfate and sulfatide synthesis, in steroid, and in phenol sulfurylation. Sulfate transfer from the activated sulfate to acceptors such as phenols, hydroxy steroids, and the hydroxy group of various compounds, and also probably amino groups, is catalyzed by enzymes which we call sulfokinases and which are more or less specific for the acceptor molecule.

This may serve as a general orientation. Now I want to discuss in detail, first, the isolation and identification of active sulfate and the enzymatic mechanism of its formation, carried out by Phillips W. Robbins (*4–6*). Then, second, I will discuss a number of sulfate acceptor reactions which have been and are being studied at the Rockefeller Institute for Medical Research by John D. Gregory, Yoshitsugu Nose, Furio D'Abramo, and Irving H. Goldberg.

Table 1. Active sulfate fraction, analytical data. Adenosine was determined by absorption at 260 mμ, ribose by the Orcinol procedure, and phosphate, by the method of Fiske and Subbarow. Total phosphate was determined by hydrolysis in 1*N* HCl acid. The 12- and 30-minute phosphate was determined by hydrolysis in 1*N* HCl at 100°C. Phosphate hydrolyzable by the 3′-nucleotidase was determined by the method of Kaplan (*21*).

Component	Amount
Adenosine	1
Ribose	0.95
Phosphate, total	1.98
Phosphate, 12-minute	0.53
Phosphate, 30-minute	1.04
Phosphate, 3′-nucleotidase	0.85
Sulfate, enzymatic	0.2–0.85

Isolation and Identification of Active Sulfate

Helmuth Hilz, with whom this venture was started, found (*7*) that the reaction between ATP and sulfate appeared to yield pyrophosphate, and, using paper electrophoresis, he could show that the compound formed contained adenylic acid. This preliminary identification was carried out by the use of radioactive sulfate. In analogy to other activation reactions, in particular to the recent studies on acetate activation, we tentatively thought of sulfate activation as a reaction between ATP and sulfate which, through a substitution of the terminal pyrophosphoryl group in ATP, led to the suspected anhydride between sulfate and substituted phosphate. However, some of the data did not fit with this interpretation, and at that stage we cautiously reported that our observations had yielded evidence for the formation of an adenyl sulfate derivative, of the exact structure of which we were not sure.

As is often the case in studies of an unknown "active" compound, especially a substance of which no chemical analog has been known before, we expected the compound to be very unstable. It had appeared, indeed, in these preliminary experiments that "active" sulfate was quite unstable to strong acid. To get a step further, it was necessary to clean up the enzymes and concentrate the sulfate activation system for use in medium-scale preparative runs (*6*); thus, Robbins succeeded in preparing 50-μmole samples of active sulfate from ATP and sulfate, and tried Dowex chromatography. Fortunately, it appeared that the phosphosulfate link was more stable to acid than had been expected; it is perfectly stable at neutral, or higher, *p*H, and it tolerated chromatography with rather concentrated formic acid in the cold. Active sulfate is strongly bound by Dowex-1, and it was possible to remove from the column all other adenine derivatives by treatment with 4*N* formic acid–0.3*M* ammonium formate. Then 5*N* formic acid–1*M* ammonium formate eluted the remaining active sulfate, and in this manner a rather homogenous fraction of active sulfate was obtained. During concentration of this fraction by lyophilization, however, part of the sul-

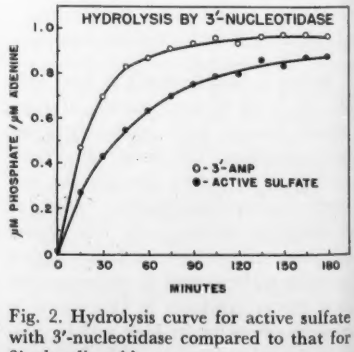


Fig. 2. Hydrolysis curve for active sulfate with 3′-nucleotidase compared to that for 3′-adenylic acid.

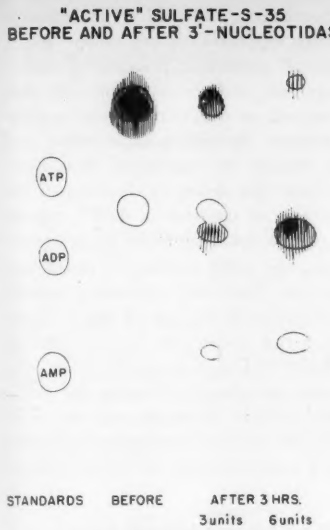


Fig. 3. Radioautogram of paper electrogram in citrate buffer of *p*H 5.9. Encircled areas are ultraviolet quenching; shaded and black areas are radioautogram tracings (see Fig. 6 in *6*).

fate was split off. The analysis of such a fraction is shown in Table 1.

It appeared from these data that the compound, to our surprise, contained two phosphates per adenine, and pentose. One phosphate was acid-stable, and the other one was unstable to heating with 1*N* HCl, but not as much so as would have been expected for a pyrophosphate link. The hydrolysis with acid rather suggested a 2′- or 3′-adenylic acid, particularly since the compound did not give the periodate reaction commonly obtained with adenosine-5′-phosphates. For further identification, Kaplan's 3′-nucleotidase was used. This enzyme liberated practically a full equivalent of phosphate from our "active" sulfate.

The active sulfate in all these cases was conveniently determined by enzymatic transfer to nitrophenol, the anion color of which disappears on conjugation.

As has been mentioned, during lyophilization part of the sulfate was split off, and this explains why the figures for sulfate in Table 1 vary between rather wide limits. Smaller batches, which could be lyophilized quickly, showed near equivalence between sulfate and adenosine. On the other hand, the sulfate-free residue gave ratios with regard to phosphate identical with those of active sulfate. In Fig. 2 the hydrolysis curve for active sulfate with 3′-nucleotidase is compared with that for 3′-adenylic acid. Hydrolysis is slower for the active sulfate than for the monophosphate; in general, the 3′-adenylic acid is the substrate most rapidly hydrolyzed by this enzyme, while additional substitutes slow down reactivity.

The position of the sulfate in the molecule was largely identified by the use of radioactive sulfate. If a mixture of active sulfate and sulfate-free residue is exposed to the 3′-nucleotidase, the sulfate remains with adenylic acid, as is shown in the paper electrophoresis pattern of Fig. 3 by the overlap of ultraviolet quenching and radiotracing. If incubated with a sufficient amount of nucleotidase, the upper spot of PAPS disappears almost completely and a new spot appears instead, which could be identified as adenosine-5′-phosphosulfate (APS). On the other hand, a lower spot appears which is adenosine-5′-phosphate (AMP), derived by hydrolysis of PAP, the sulfate-free residue. The adenosine-5′-phosphosulfate could be identified by comparison with synthetic compound, prepared according to the method of Baddiley *et al.* (*8*). The structure and some of the properties of the active sulfate are explained in Fig. 4, where it may be seen that the phosphosulfate link is rather sensitive to hydrochloric acid; 0.1*N* HCl split the sulfate completely off in about half an hour at 37°C. These compounds have an ultraviolet absorption indistinguishable from that of adenylic acid. This excludes any possibility of sulfate being linked to the amino group of adenine, since blocking of this amino group in all cases causes a shift of the ultraviolet absorption toward the visible.

For further identification, we argued that hydrolysis of the phosphosulfate link should liberate a secondary phosphate. This was shown to be the case by means of electrotitration between *p*H 5 and 8 before and after hydrolysis. All this evidence makes us feel sure that we are dealing with a compound of the constitution shown in the figures. This constitution has now been confirmed through synthesis by Baddiley *et al.* (*9*).

Two Enzymatic Steps in Biosynthesis of Active Sulfate

The unexpected appearance of two separately linked phosphates in the active sulfate, as now identified, indicated right away a two-phasic synthesis as likely. Initially, we had speculated (*7*) on the possibility of adenosine-5′-phosphosulfate being active sulfate, formed by pyrophosphate substitution on ATP. It now appeared that this reaction was the first step in the sequence shown in Fig. 5. This was completed by a second reaction, of phosphokinase type, whereby the terminal phosphate of a second ATP was transferred to the 3′-position of APS. The initial reaction is catalyzed by an enzyme which we call sulfurylase. It catalyses the attack of one of the oxygens of sulfate on the proximal phosphorus in adenosine-5′-triphosphate with

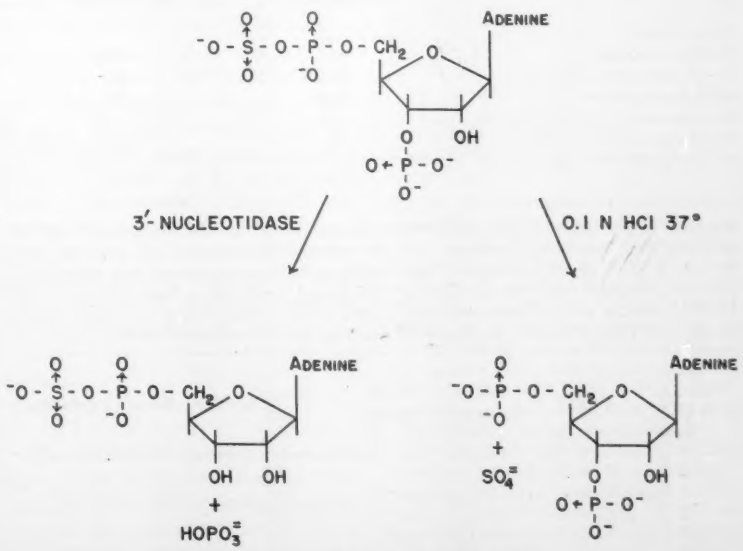


Fig. 4. Active sulfate and hydrolysis products.

the displacement of pyrophosphate by sulfate. The APS, thus formed initially, in *entirely inactive* as a sulfate donor in enzymatic reactions.

It is important to realize that the reaction as written is actually much more favored energetically in the backward direction; in other words, the sulfuryl potential in APS is considerably higher than the pyrophosphoryl potential in ATP. We believe that this energetic situation is the reason for the further phosphorylation. In this manner, the energy of a second energy-rich phosphate is used to force the reaction into the forward direction by a "masking" of the reaction product through 3′-phosphorylation. The over-all energy balance, even then, is not too favorable, and the rather energy-rich phosphosulfate bond becomes still further stabilized through removal of the initial reaction product, pyrophosphate, by the quite ubiquitous pyrophosphatase.

In proving this mechanism, the independent work of Bandurski *et al.* (*10*) has been rather important. These workers found that the sulfate activation system in yeast could be separated into two inactive fractions, active only after recombination. When Bandurski's work came to our attention, we turned to the yeast system for elaboration of the mechanism, as it appeared preferable to the liver system we had used so far. Confirming Bandurski, we were able to separate from yeast two fractions, which were identified with (i) sulfurylase, and (ii) APS-kinase.

Sulfurylase was measured, as is indicated in Table 2, in the reverse direction by means of synthetic APS. Sulfurylase from yeast could be rather highly purified by electrophoresis on Geon 426, as is shown in Fig. 6. With this purified enzyme, equilibrium studies were made which showed that, as seen in Fig. 7, a small but definite amount of APS was formed in the forward direction. The equilibrium constant for the reaction

$$ATP + S \rightleftharpoons APS + PP$$

at *p*H 8 is approximately 10^{-8}, and therefore $\Delta F°$ equals 11,000 cal. But APS was found to have a high affinity to APS-kinase, giving, indeed, the highest reaction rate at the lowest measurable concentration, $5.10^{-6}M$. The amounts formed enzymatically are, under "physiological" conditions, probably of similar magnitude, and therefore the little that is formed can thus immediately be phosphorylated by APS-phosphokinase and can thereby be eliminated from equilibrium. This drives the reaction in the direction of synthesis of PAPS, helped by pyrophosphatase, removing pyrophosphate, the other product of sulfurylase reaction. There are interesting general implications in this use of two or more energy-rich phosphates for the fixation of bonds of higher group potential, such as the phosphosulfate bond, the additional energy serving to pull an initially-formed, thermodynamically very unstable compound over the energy hump:

$$ATP + S \xleftarrow{\text{sulfurylase}} APS + PP \qquad \Delta F°, +11{,}000 \quad (4)$$

$$PP \xrightarrow{\text{PP-ase}} 2P \qquad \Delta F°, -5{,}000 \quad (5)$$

$$APS + ATP \xrightarrow{\text{APS-kinase}} PAPS + ADP + H^+ \qquad \Delta F°, -6{,}000 \quad (6)$$

$$2ATP + S \rightarrow PAPS + 2P + ADP \qquad \text{over-all} \quad \Delta F°, \quad 0 \quad (7)$$

The energy data are rough approximations, to give an impression of the over-all $\Delta F°$, which, taking into account the formation, at *p*H 8, of H^+ as calculated for hexokinase in (*11*), just about balances.

Table 2. Separation of yeast enzymes. National Bakers yeast was used, and extracts were prepared essentially according to the method of Jones *et al.* (*22*). The formation of ATP from APS was measured by following pyrophosphate disappearance or by measuring ATP formation with hexokinase and glucose-6-phosphate dehydrogenase. Formation of PAPS was followed by transfer to nitrophenol or by PAP assay. The PAP assay depends on the catalytic activity of PAP in the transfer of sulfate from *p*-nitrophenol to phenol. The rate of nitrophenol formation is measured at 400 mμ in the Beckman DU spectrophotometer. The reaction between APS and P was routinely followed by measuring the disappearance of P with chromatographic checks on ADP formation.

Fraction	ATP-sulfurylase (APS + PP → ATP) − PP, (μmole/mg hr)	APS-kinase (APS + ATP → PAPS) PAPS, (μmole/mg hr)
Dialyzed extract, I	2.1	
NaCl precipitate, II	10.1	0.55
17–23 percent EtOH, III	22.1	3.5
*p*H 5.4 precipitate, IVa	85.0	0.6
Supernatant + 10 percent EtOH, IVb	0.5	4.1
40–50 percent $(NH_4)_2SO_4$, V	0	12.5

Table 3. Sulfate transfer from $PAPS^{35}$ to chondroitin sulfate. The enzyme preparation, prepared from three chick embryos, as in the previous experiments, was extracted with 6.5 ml of saline-phosphate solution and centrifuged. The supernatant was mixed with 0.25 ml of $PAPS^{35}$, and 1 ml was immediately heated (zero time). Each tube contained 1 ml of enzyme in a 1.35-ml total and 15,000 counts. Precipitation was with sodium acetate and 3 vol of alcohol; there were 10 washings with 80 percent alcohol.

Incubation (37°C) (hr)	$PAPS^{35}$	ATP 1 μmole	UTP 1 μmole	Count/min	Δ	Incorporation (%)
0	+	−	−	80		
2	+	−	−	340	260	1.7
2	+	+	−	600	520	3.4
2	+	−	+	670	590	4
2	+	+	+	550	470	3

Transfer of Active Sulfate to Various Acceptors

With the solution of the problem of sulfate activation, the way had been opened to approach more intelligently the metabolic utilization of sulfate. This, in a sense, forced us to enter metabolic territory rather foreign to the experience of workers in our laboratory—some steroid metabolism but, more seriously, polysaccharide synthesis and lately some lipid chemistry. Generally, in these experiments, isolated PAPS was not used, but rather PAPS was fed in by way of an enriched enzymatic generating system from yeast (*5*) or liver (*6*). For confirmation, the various acceptor reactions were then checked with isolated PAPS.

Except in the case of phenol and steroid conjugation, we are still in the more exploratory phase, using almost exclusively S^{35} as a guide. We have made available cell-free preparations from embryonic cartilage for synthesis of chon-

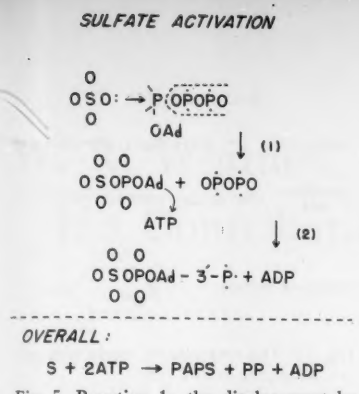


Fig. 5. Reaction 1: the displacement by sulfate of pyrophosphate in ATP, yielding APS, is catalyzed by sulfurylase. Reaction 2: the phosphorylation of APS by the terminal phosphate of ATP is catalyzed by APS-phosphokinase.

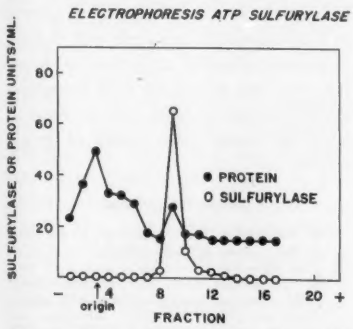


Fig. 6. Electrophoresis in a Geon 426 (Goodrich) bed (see Fig. 8).

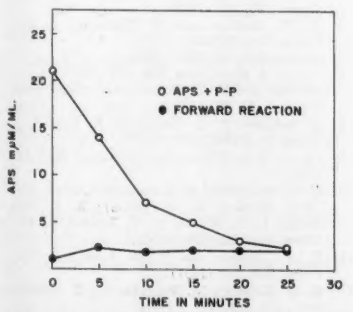


Fig. 7. Equilibrium experiment; ATP-sulfurylase.

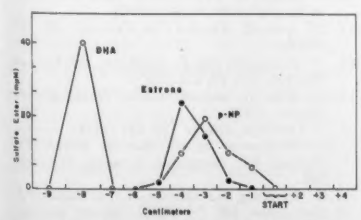


Fig. 8. Electrophoresis of rat enzymes in a Geon 426 (Goodrich) bed.

droitin sulfate, and from rat liver and brain for synthesis of sulfatide, but many needed details are still missing.

For orientation, I would like to refer once more to Fig. 1, in which it may be seen that, after resolving the left and middle part of the scheme, which concerns the generation of active sulfate, we now move into the nearly virgin territory of sulfate utilization outlined in the right-hand part of the figure.

Conjugation of Steroids and Phenols

This reaction has been studied by DeMeio (*12*), and by Roy in England (*13*), and we have used the latter's method for the estimation of sulfurylated steroids. Y. Nose, from the University of Kyoto, has worked in my laboratory on the separation of the enzymes responsible for the conjugation of phenols and polycyclic acceptors, using mainly electrophoresis of a prepurified liver preparation. It may be seen in Fig. 8 (*14*) that by this means three enzyme fractions were obtained, one for dihydroandrosterone and other 3′-β-OH steroids. Another enzyme conjugates with estrone and is different from ordinary phenol-sulfokinase. The last-named, however, seems to accept sulfate relatively unspecifically on a great variety of variously substituted phenols, as elaborated in greater detail by John D. Gregory (*15*). The dihydroandrosterone sulfokinase also reacts with isoandrosterone and with progesterone, all having a 3′-β-hydroxyl. It therefore appears to be a 3′-β-hydroxysteroid sulfokinase.

It should be mentioned that in nitrophenyl sulfate, the sulfate group was shown by John Gregory (*15*) to be of a group potential only less than 2000 calories below that of PAPS; a PAP-mediated sulfate transfer from nitrophenol to phenol has been studied with phenol-sulfokinase. Nitrophenyl sulfate was also shown, by Egami and his collaborators (*16*), to act as sulfate donor in a sulfatase-catalyzed, PAP-independent reaction, which reminds one of the rather outstanding activity of nitrophenyl phosphate for donating phosphate unspecifically with phosphatase (*17*).

Synthesis of Chondroitin Sulfate

The structure of chondroitin sulfate is presented in Fig. 9, for orientation. After unsuccessfully trying various cartilage preparations, which had been shown by other workers to incorporate radioactive sulfate in chondroitin sulfate in in vivo or in slice experiments, we turned to embryonic cartilage from 15-day-old chick embryos, which yielded rather active nonparticulate extracts. Figure 10 shows that active sulfate was formed in such an extract, together with small amounts of the precursor APS; in this experiment, the charcoal absorbate of the incubate was eluted with pyridine and then put on the paper for electrophoresis.

Chondroitin sulfuric acid was isolated by the usual methods of precipitating

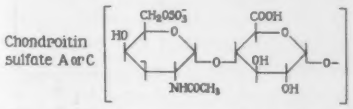


Fig. 9. Repeating unit of chondroitin sulfate.

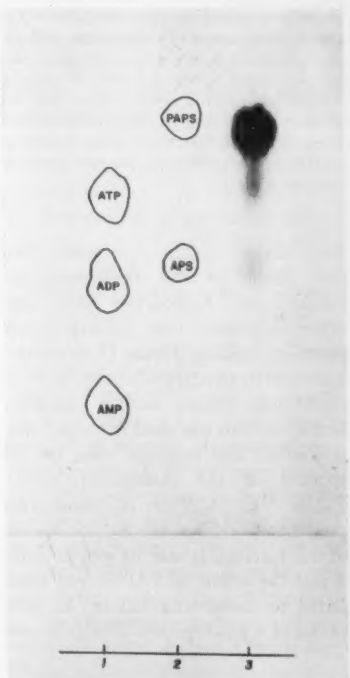


Fig. 10. Radioautogram of paper electrogram from $SO_4^{35=}$ incubated cartilage extract. Cartilages from two embryos were homogenized in 3 ml of saline phosphate to which 12 μmole of Mg^{++}, 10 μmole of Na-ATP, 1.5 μmole of UTP, 2 μmole of glutamine, 2.7 ml of enzyme, and 2 ml of $SO_4^{35=}$ (100 μc, carrier-free) were added; the total volume was 5.3. The mixture was incubated for 2 hours at 37°C. Markers electrographed on the same paper strip are identified in radioautograms Nos. 1 and 2 by ultraviolet quenching, as indicated by encircling lines. Number 3 represents the radioautogram of paper electrogram in citrate buffer (*p*H 5.9) of the pyridine eluate from a charcoal adsorbate of incubate.

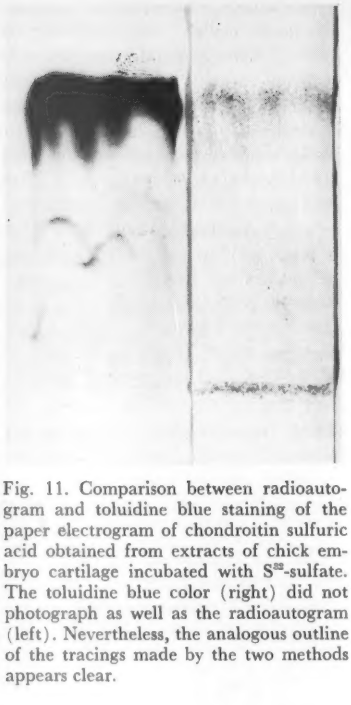


Fig. 11. Comparison between radioautogram and toluidine blue staining of the paper electrogram of chondroitin sulfuric acid obtained from extracts of chick embryo cartilage incubated with S^{35}-sulfate. The toluidine blue color (right) did not photograph as well as the radioautogram (left). Nevertheless, the analogous outline of the tracings made by the two methods appears clear.

from acetate-containing solution either with alcohol or with cetyltrimethylammonium salt. Radioactive sulfate and other compounds were removed by appropriate washing. Figure 11 shows that radioactivity overlapped exactly with the chondroitin sulfuric acid; a phosphate buffer medium was used for paper electrophoresis and toluidine blue, for the spotting of the chondroitin sulfate. Tables 3 and 4 (from *18*) show some preliminary studies on the mechanism of this reaction. It may be seen in Table 3 that the sulfate of PAPS[35] was transferred to chondroitin sulfate. An indication of a participation of uridylic acid in the synthesis may be seen in the slightly better activation, in this case, when UTP was used instead of ATP. In other experiments, however, UTP was often inhibitory. Table 4 shows that with these extracts, ATP and magnesium were necessary for chondroitin sulfate synthesis from inorganic sulfate. This was also true if isolated PAPS was used, confirming the *de novo* synthesis of polysaccharide. Further evidence for *de novo* synthesis of chondroitin sulfate in these extracts was obtained by showing incorporation of radioactive acetate.

A great deal remains to be done. The polysaccharide field is a vast area of chemistry, and I have to confess that it is not our intention to become polysaccharide chemists. However, we will try to stay with this type of reaction for a little while, since it has been forced on us through our progress with sulfate activation. For similar reasons, we ventured also into the equally complex field of lipid synthesis. Irving Goldberg is studying in vitro incorporation of sulfate into lipid fractions. He has obtained preliminary evidence of a formation in liver extracts and brain homogenates of a sulfatide similar to Blix's cerebroside sulfate (*19*), shown in Fig. 12. This problem seemed attractive to me mainly because we might, from present experience, anticipate here a direct transfer of a galactose sulfate derivative to ceramide. This would present a simpler metabolic sequence than chondroitin sulfate synthesis, which is complicated by the polymerization problem. That, however, makes the latter all the more challenging.

Finally, I would like once more to underline the fact that we are dealing, in the area of sulfate transfer, with a process in which a central activated

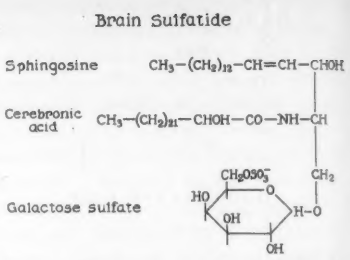


Fig. 12. The structure of cerebroside sulfate according to Blix (*19*).

molecule is first elaborated. This carries the sulfate in activated form, and from there, sulfate is picked up by quite a large number of separate acceptor enzymes which we call sulfokinases. This is a repetition of a rather general scheme in biosynthesis. It has been well defined in the case of acetyl activation and transfer (*20*) and, of course, with phosphate activation and transfer, and it seems to apply in many other cases of group transfer.

Table 4. Incorporation of $S^{35}O_4^=$ into chondroitin sulfate. Condyles from tibias and femurs of three chick embryos were broken up in deep-freeze-cooled mortar with quartz sand, with 6 ml of saline and 0.01*M* phosphate (*p*H 7.4), and centrifuged at 6000*g* (International centrifuge) for 10 minutes. The supernatant was mixed with 1.2 ml of carrier-free $S^{35}O_4^=$ (60 μc). There was 1 ml of enzyme-S^{35} mixture in each sample; final volume was 1.35 ml.

Sample No.	Incubation (37°C) (hr)	ATP 5 μmole	Mg 6 μmole	Glutamine 1 μmole	UTP 1 μmole	Counts/min	%
1	0	−	−	−	−	60	
2	2	−	−	−	−	60	
3	2	+	−	−	−	405	
4	2	+	+	−	−	4760	0.6
5	2	+	+	+	−	5390	0.7
6	2	+	+	+	+	2007	0.28

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2. The following abbreviations have been used in this article: ADP, adenosinediphosphate; AMP, adenosine monophosphate; APS, adenosine-5′-phosphosulfate; ATP, adenosine triphosphate; CoA, coenzyme A; P, inorganic phosphate; PAP, 3′,5′-diphosphate; PAPS, adenosine-3′-phosphate-5′-phosphosulfate (active sulfate); PP, pyrophosphate; S, sulfate; UTP, uridine triphosphate.
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W. R. Whitney, the Man and His Contribution to Science

Willis Rodney Whitney was a perfect example of what may be called the ideal scientist—perhaps one should say the experimental scientist, because he had a passionate love of experiment. Keen, imaginative, bold, with insatiable curiosity, he literally worshipped the search for truth. It was said of him that if he had elected to pursue the solitary path of an inventor, he doubtless would have become one of the world's most famous and prolific inventors.

However, he sacrificed this opportunity for a greater service—the organization and successful direction of the first industrial research laboratory in the country devoted to fundamental research. This was a truly pioneer task. Industrial laboratories at that time were almost exclusively devoted to product development and improvement. Fundamental research was confined to universities. Could it be done profitably in an industrial laboratory? E. W. Rice, at that time chief engineer of the General Electric Company, had the vision that it could.

Dr. Whitney was well started on a successful career of teaching and research at Massachusetts Institute of Technology, and had already made important contributions to colloid chemistry, when Rice visited him and made the proposal that he start a research laboratory at General Electric. Rice proposed that it should combine fundamental with applied research—a new and bold idea. At first Dr. Whitney demurred, for he was happy in his work at M.I.T. But in response to Rice's quiet persistence, he finally agreed to try it on an experimental basis, for he loved an experiment. He agreed to spend three days a week at General Electric, commuting between Schenectady and Boston.

Whitney's first laboratory was a barn in the rear of Steinmetz' house, and his staff consisted of himself and one part-time assistant, whom he shared with Steinmetz. The next year he moved to a room in the Schenectady works and began gradually to build up a staff. For three years he continued to commute, until he was finally convinced that this research "experiment" held sufficient fascination to enlist his wholehearted devotion. It was typical of Rice that he did not choose an organizer. Dr. Whitney was not an executive type. He hated routine. Conferences and committees bored him. Budgeting and bookkeeping were not among his interests. Nor had he that passion for being "at the head of something" that characterizes many leaders. What Rice saw in Dr. Whitney was the *scientist*, whose enthusiasm for research was infectious.

Dr. Whitney's organization of the laboratory and his method of operating it were unique, and resulted from his many remarkable personal qualities. In organizing the laboratory, he proceeded in the same manner as he did in his scientific experiments. He began cautiously, on a small scale, feeling his way. In expanding, he always moved more slowly than his directors urged him to do.

One of the first qualities needed was tact, to induce experienced company managers to accept help from this college highbrow. Dr. Whitney's attitude of learner, which was genuine, soon won their confidence.

Sound judgment told him that the laboratory must, first of all, be made to pay. He personally directed high-temperature treatment of lightning arrester pellets, carbon brushes, and carbon lamp filaments, all of which produced useful improvements. Then came Coolidge's ductile tungsten, and the laboratory's success was firmly established.

Such success might have turned the head of a less idealistic man. To Whitney, it was just a necessary preliminary to the real purpose of the laboratory, as he saw it, which was fundamental research. He engaged Irving Langmuir and gave him freedom to work on anything that interested him. After three years, Langmuir was still deep in a study of heat conduction in gases. With no practical applications in sight, the board of directors questioned the advisability of keeping him. Dr. Whitney replied unhesitatingly and emphatically: "You leave Langmuir alone. He is doing good work." The results were soon to prove it.

Such personal modesty and confidence in human nature, which led him to allow those members of his staff whom he considered qualified to work on what interested them, were the most significant features of Dr. Whitney's direction and were in large measure responsible for the success of the laboratory. However, he didn't just leave these researchers alone. He made daily rounds of the laboratory, encouraging and suggesting, but seldom dictating or criticizing. He always had a stock of new suggestions for experiment, which he literally peddled from room to room, but seldom assigned.

Dr. Whitney was a pioneer in championing prompt and full publication of laboratory results, subject only to filing of patent applications. Such results always appeared in the name of the individual worker, for Whitney never allowed his own name to appear. Because of this characteristic modesty, his own contributions, which were great, will never be fully known. For example, he suggested and directed the research on hydrogen cooling of generators but insisted that all the credit should go to the man who did the work. Only two inventions he could not escape claiming: the "metallized" carbon filament, his early work; and the inductotherm, which he personally developed.

The most important factor in the success of Dr. Whitney's direction was the fine spirit of honesty, cooperation, and enthusiasm, which he was very careful to preserve as he gradually built up the laboratory staff. This spirit was part of himself, and it spread by contagion as he made his daily rounds. Discipline was unnecessary. As one employee expressed it: "The meanness or selfishness of our natures never had a chance to get out. We were ashamed to show it." His office door bore the sign: "Come in—rain or shine," and the janitor or office boy was welcomed with the same genuine interest as a department manager.

Dr. Whitney's most characteristic quality was his love of research, which he considered the "finest of sports." His standard greeting on his daily rounds was: "Are you having any fun?" Scientific curiosity, which he once defined as the most important quality of a research man, was a passion with him, and his leisure hours on his farm were filled with experiments.

A man's true personality can often best be understood from an observation

of his leisure activities. These may include fishing, hunting, golf, driving around the country, movies, television, and bridge. Dr. Whitney had none of these hobbies. His one consuming interest was the study of nature, for which his curiosity knew no bounds. He studied the habits of turtles, where they laid their eggs, where they spent the winter, and how often they returned to the same place, by marking them with the place and date; how mosquitoes knew what to bite, by counting the number that lighted on him, and on a quarter of beef beside him; what caused galls to grow on golden rod, by inserting a piece of iron wire and heating it with high frequency; what caused cockroaches to enter a trap, by counting the numbers caught in two bottles, one of which contained sugar. His occasional walks along the Mohawk River were devoted to a search for Indian arrowheads, which he could find when no one else could. He kept careful notes of these experiments and also of ideas that came to him in his reading and thinking.

Dr. Whitney spent all his days at the laboratory, where he was always the first to arrive in the morning. But his evenings were devoted to scientific reading. He was a voluminous reader, especially in physics, chemistry, biology, and the history of science; and the range of his knowledge and interest was correspondingly wide. Fittingly, the new library at the General Electric Research Laboratory has been named the Whitney Library.

ALBERT W. HULL
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News of Science

National Aeronautics and Space Administration, Its Administrator and Deputy Administrator

In the matters that come before it, the Congress of the United States sees a variety of subjects ranging from the ludicrously insignificant to the critically important. The committees and the full bodies of the House and Senate can on one day ponder the implications of letting the Girl Scouts use Army equipment and on the next consider the problem of Presidential disability. The legislative hopper is commodious and indiscriminate. If the 85th Congress has had its share of "little" bills, it has also deliberated on many major measures that rank with the Atomic Energy Act and the National Science Foundation Act in the matter of far-reaching significance. The National Aeronautics and Space Act of 1958 constitutes such a measure in its import, to both science and the national security. In its handling of the President's proposal for this act and his recommendations of men to fill the two top posts, Congress has moved quickly, intelligently, and with an unusual awareness of the implications of the legislation at hand.

National Aeronautics and Space Act

On 29 July the President effected Public Law 85-568 by signing a House of Representatives bill sent to him by the Congress. The law declares that "it is the policy of the United States that activities in space should be devoted to peaceful purposes for the benefit of all mankind" and that "the general welfare and security of the United States require that adequate provision be made for aeronautical and space activities." To accomplish these ends the law calls for the establishment of three new governmental units, an Aeronautics and Space Council, an Aeronautics and Space Administration, and a Civilian-Military Liaison Committee. The council, to be headed by the President of the United States, will have as members the Secretary of State, the Secretary of Defense, the Administrator of the NASA, the Chairman of the Atomic Energy Commission, and four other presidentially appointed persons, one from the Federal Government and three from among "individuals in private life who are eminent in science, engineering, technology, education, administration, or public affairs." The council will advise the President on the broad outlines, both present and future, of aeronautical and space activities in the country.

The Administration. The Aeronautics and Space Administration will have three major functions. As these appear in the law, they require that the administration shall: "(1) plan, direct, and conduct aeronautical and space activities; (2) arrange for participation by the scientific community in planning scientific measurements and observations to be made through use of aeronautical and space vehicles, and conduct, or arrange for the conduct of, such measurements and observations; and (3) provide for the widest practicable and appropriate dissemination of information concerning its activities and the results thereof." For the performance of its functions the administration is granted many of the usual powers given to federal agencies and two unusual ones that are interesting in their departure from normal procedure. The first of these departures allows the administrator to appoint up to 260 scientific, engineering, and administrative personnel without regard to the civil-service laws, and to compensate them without regard to the Classification Act of 1949. This exemption allows the administrator to staff his agency with highly qualified men and women by enabling him to offer salaries of up to a limit of $19,000 a year, or up to a limit of $21,000 a year for a maximum of ten positions. A second significant departure authorizes the administrator to employ aliens without regard to statutory provisions prohibiting payment of compensation to such persons. This would seem to be a significant exemption in that it makes available to the administration the services of any European or other foreign scientist who might be interested in working on one or another of the projects that are undertaken in the future.

Jurisdiction. The significant matter of jurisdiction over projects as it relates to the new administration and the Department of Defense received detailed attention by the congressional framers of the act. It was recognized that activities which are peculiar to or primarily associated with weapon systems or military operations or to the defense of the United States (including the research and development necessary to make effective provision for the defense of the United States) should be under the jurisdiction of the Department of Defense, while all others should be under

the administration. But in projects which at the basic concept level were not clearly assignable to the administration or the defense establishment it was felt that coordination at the highest governmental levels was necessary. Accordingly, the act makes two provisions to aid in determining jurisdiction. First, the President, advised by the council, is given the responsibility of assigning specific projects to the proper group. Second, the act provides that the administrator of the National Aeronautics and Space Administration and the Secretary of Defense can seek solutions to questions of jurisdiction either directly or through the Civilian-Military Liaison Committee to hold to a minimum the questions referred to the President and the council. Allowance is also made for cooperative work on projects which are determined to be of sufficient joint interest.

National Advisory Committee for Aeronautics. The circumstances under which the administration will be organized are particularly fortunate in one regard. Rather than having to organize in the void, so to speak, the men that set up the working administration will have a 38-year-old core on which to build. This core, the National Advisory Committee for Aeronautics, now headed by Hugh L. Dryden, who will become the deputy administrator of the new agency, has a long and productive history of work with governmental agencies, particularly the Department of Defense and its predecessors. The utilization of the old agency as the basis for the new will make for a continuity of records, administrative procedures, and to some extent, of personnel and policy.

The Administrator

To fill the top position of the new agency, that of administrator, President Eisenhower recommended Thomas Keith Glennan, president of Case Institute of Technology in Cleveland, Ohio. The Senate, after brief hearings by its committee on space and astronautics, confirmed the nomination unanimously and without debate. Glennan, who reached his fifty-third birthday 4 days ago, was born in Enderlin, N.D., the son of a train dispatcher. Most of his youth was spent in Eau Claire, Wis., where he attended high school and, for 2 years, State Teachers College. In 1924 he entered Yale University and, because of his earlier college work, graduated 3 years later from its Sheffield Scientific School with a B.S. degree in electrical engineering. Between graduation and the war years Glennan worked with various motion picture companies, Western Electric, and Vega Airplane Corporation. He joined the Columbia University division of war research in 1942, serving through the war, first as administrator, and then as director, of the Navy's Underwater Sound Laboratories at New London, Conn. For these services he was awarded the Medal of Merit. At the end of the war he became an executive of Ansco. From this position he was called to the presidency of Case. His previous work in government was with the Ordnance Panel of the Research and Development Board, the Atomic Energy Commission as a commissioner, for 2 years, and with the McKinney Panel on Peaceful Uses of Atomic Energy and the Hayworth Committee on the Evaluation of the Combat Development Program of the Army, as a member in both cases.

T. Keith Glennan

Hugh L. Dryden

The confirmation hearing before the Senate committee was characterized by amiability and good will on the part of the Senators and the nominee. Senators Johnson and Green did most of the significant questioning, inquiring into matters such as possible conflict of interest, definition of the role of the administrator, and the state of American scientific and educational activities as they compare with Russian activities. All of these matters were resolved to the committee's satisfaction. In answer to Senator Green's question about the primary requisites of the job, Glennan made this statement: "Application and understanding, I think, of the manner in which some of these things get done. It isn't just a matter of the money that is involved, but it is a matter of the people involved and how one can best motivate the people to highest performance." Senators Bricker, Anderson, and Hickenlooper had no questions to ask the nominee, but did express their gratification at Glennan's selection, willingness to serve, and his return to government service. Those who commented most fully on the nominee were ones who had worked with, or known him, during his 2-year tenure as a commissioner of the AEC.

The Deputy Administrator

The National Advisory Committee for Aeronautics will be the core of NASA. Its director for the past 11 years, Hugh Latimer Dryden, will become the deputy administrator of the new administration, serving directly under T. Keith Glennan. Dryden, who has been in government service since 1918, came to NACA from the National Bureau of Standards, where he had been associate director. Some of his early laboratory work at the bureau served as the basis for his Ph.D. from Johns Hopkins, which was awarded in 1919. Born 2 July 1898 in Pocomoke City, Maryland, the son of a streetcar conductor, which, as he said to the Senate Committee, gives him some kinship with Glennan, he was reared in Baltimore, where he attended the public schools and the undergraduate college of Johns Hopkins. His postdoctoral work at the Bureau of Standards was centered chiefly on aerodynamics. In 1920 he became head of the bureau's aerodynamic section. In connection with his work in this field, fluid mechanics, acoustics, and others, he has published more than 100 technical papers and articles in professional journals. As head of the "Washington project" of the National Defense Research Committee he led development of this country's first and only guided missile successfully used in combat, the radar-homing Bat. This achievement won him the Presidential Certificate of Merit in 1948. Dryden is a member of many scientific groups, including the AAAS. In 1949 he served as president of the Cosmos Club.

As a result of his long association with the Government and various military projects, Dryden has often been called on to speak on some aspect of scientific work with which he is acquainted. Addressing the California Wing Convention earlier this year, he briefly examined

the statutory separation of civilian and military projects under the enabling legislation of the NASA and the jurisdictional problems involved. He commented: "I, for one, might be concerned about the difficulties that could be expected to arise in these negotiations, were it not that since 1915 the military services and the NACA have worked together—closely and harmoniously. The fact that we are moving into the new unexplored areas of space merely increases the essentiality of this effective partnership." In other talks Dryden has given examples of this civilian-military cooperation. Before the House Select Committee on Astronautics and Space Exploration he cited two examples of such work, both involving military missiles. They were the development of the "blunt-nose" concept for the design of missile warheads and the wind-tunnel tests which identified the gas eddy phenomenon which was destroying the early Jupiter missiles.

The new Deputy Administrator of the National Aeronautics and Space Administration, in accord with his long experience and extensive familiarity with the problems involved, is not given to sweeping statements on future developments in space activities. His attitude can best be seen in his closing words to the House Committee: ". . . I should like to echo the thought expressed by Dr. Killian and his committee, that we should be 'cautious and modest in our predictions and pronouncements about future space activities . . . and quietly bold in our execution.' "

Lysenkoism Again?

The character of Soviet participation in the International Congress of Genetics that took place recently in Montreal changed sharply just before the congress was to open. Last-minute cancellations were received from several scheduled speakers. At the same time, the Soviet delegation submitted further titles of papers to be delivered, so that the Soviet contributions to the meeting were predominantly of the controversial Lysenko school of genetics. Earlier it was thought that studies based on both the Lysenko school and on points of view closer to classical Western genetics would be reported by the Russians. (It has been rumored that several geneticists from East Germany who had intended to come to the congress had been unable to obtain exit permits for the trip.)

Trofim D. Lysenko, who rose to a position of power in Soviet science under Stalin, holds that in some cases acquired characteristics can be passed on to future generations. His views are in conflict with those of most Western geneticists. In recent years Lysenko's influence seemed to have waned.

As a result of the Soviet delegation's program changes, the Permanent International Committee for Genetics Congresses passed the following resolution on 25 August and presented it to the final plenary session of the Montreal congress.

"The Permanent International Committee on Genetics Congresses considers it to be its duty to express deep concern over the fact that a number of Soviet geneticists who had submitted abstracts of papers to the X International Congress of Genetics failed to appear in Montreal. The Committee also deeply regrets the absence of representatives at the Congress of a number of other countries. It wishes to express its deepest sympathy and sends its warmest regards to all scientists who may have been prevented from attending the Congress by their governments.

"The IX International Congress of Genetics, meeting in Bellagio in 1953, passed a resolution that Genetics Congresses should not 'be held in any country to which it may be expected that scientists would be refused permission to enter on grounds of race, nationality, religion, place of birth, or political associations past or present.' The Permanent Committee takes this occasion to extend this policy by appealing strongly to all governments in the world to allow their scientists the right of unimpeded travel for scientific purposes, without regard of race, nationality, religion, place of birth, past or present political associations and, in view of the experiences at the current Congress, irrespective of whether their scientific views and work are in conformity with any official governmentally-shaped policies and ideology. We consider any attempt on the part of governments to interfere on political, ideological or other grounds with the free pursuit of science and free dissemination of scientific information as a serious violation of the basic principles of research. We appeal to the learned academies and scientific societies of all countries and to the United Nations and its organizations to exert all possible influence to persuade all governments to adhere to the principles outlined here. Their violation will, no doubt, spell the end of scientific freedom and therefore also of scientific progress."

School and College Enrollment

The nation's total school and college enrollment, increasing for the 14th consecutive year, will reach a new all-time peak of about 45 million in school year 1958–59, according to the U.S. Office of Education. One of every four persons in the United States will attend school or college. Enrollment will be about 1,750,000 higher than the previous record enrollment of 43,195,000 last school year.

Public and private school enrollment in kindergarten through grade 8 is expected to total about 31,793,000, a gain of more than a million over last year's elementary school enrollment of 30,670,000.

A gain of almost half a million is expected in high school (Grades 9 through 12), with an enrollment of 8,880,000 in 1958–59 compared with 8,424,000 last year. For every 100 persons aged 14–17 years, 83 persons will be enrolled in high school. Ten years ago 75 in 100 were enrolled.

Colleges and universities are expected to enroll about 173,000 more students during the coming academic year than they did last year—3,623,000 this year, 3,450,000 last year.

Approximately 245,500 additional qualified teachers are needed this year 99,000 to replace teachers who died, retired, or left the profession to be married or take other employment last year; 55,000 to meet requirements of increased enrollments; and 91,000 to replace emergency teachers.

It is estimated that 90,300 men and women will enter the teaching profession for the first time this year and that 23,000 former emergency teachers will have attained qualified status. The remaining shortage of 132,200 will be met by a return to teaching by former teachers, by the employment of emergency teachers, and by the establishment of excessively large classes.

Neutron Cross Sections

A second, completely revised edition of BNL-325, *Neutron Cross Sections*, has been prepared at the Brookhaven National Laboratory. BNL-325, successor to the compilation AECU 2040, was originally prepared for the first International Conference on the Peaceful Uses of Atomic Energy at Geneva in 1955. Since then, it has been widely distributed by the Superintendent of Documents and has become the standard reference handbook of neutron cross sections. The second edition of BNL-325, available at the second International Conference in Geneva this month, will be put on sale by the Government Printing Office.

Of interest to reactor specialists and nuclear physicists alike, this second edition of BNL-325 contains carefully evaluated data on thermal cross sections and resonance parameters, as well as curves of partial and total cross sections as functions of energy. This work is international in coverage and includes the most recent data available from many laboratories throughout the world.

Senses on TV

"Gateways to the Mind," over NBC television at 8 P.M. on 23 October, will deal with the operation of the human senses. Wilder Penfield, director of the Montreal Neurological Institute, will appear on the program to explain his work in eliciting sensory impressions by direct stimulation of the brain. Hadley Cantril, psychologist at Princeton University, will show some of his experiments in sensory illusion. George Wald of the Harvard University Biological Laboratories and Frederick Crescitelli, zoologist at the University of California, Los Angeles, served as advisers for the program, which was produced under the supervision of a 10-man scientific advisory board as part of the Bell System Science Series.

News Briefs

The University of Michigan's new Mammalian Genetics Center opened this month under its newly appointed director, geneticist Morris Foster. The center is one of three in the United States set up by the National Institutes of Health, U.S. Public Health Service. Others are located at the University of Kansas and the University of Miami (Fla.).

* * *

The ground-breaking ceremony for the Smithsonian Institution's Museum of History and Technology took place at the end of August. The new museum, which was authorized by Congress in June 1955, will be of contemporary design but will retain a classical spirit so that it will harmonize with existing buildings. It will house historic and scientific collections totaling more than a million and a half specimens, only a small fraction of which can now be displayed in existing Smithsonian buildings.

* * *

Completing a first decade of research support, the American Heart Association has announced that a total of approximately $8 million will be expended for scientific studies in the field of the heart and blood vessel diseases during the 1958–59 fiscal year. This is the largest sum the association and its affiliates have ever spent for cardiovascular research during a single 12-month period.

* * *

An 8-page supplement to the National Bureau of Standards handbooks dealing with radiation protection and related matters has been prepared by the National Committee on Radiation Protection and Measurements (NCRP). Entitled "Maximum Permissible Radiation Exposures For Man," the supplement summarizes the new recommendations of the NCRP on safe limits of radiation exposure. The new publication introduces only minor changes and is intended to be in general conformity with the philosophy expressed in the April 1956 statements of the International Commission on Radiological Protection (ICRP).

* * *

Funds for construction and equipment of the National Library of Medicine were voted by the House and Senate on 18 July in a bill covering 1959 appropriations for the Departments of Labor, and Health, Education, and Welfare, and related agencies (HR 11645). The President signed the bill on 1 August as Public Law 85-580.

* * *

A large and valuable collection of ethnological specimens, including some 6500 objects representing the cultures of peoples of many groups of islands in the Pacific, has arrived at the Chicago Natural History Museum. The Pacific Collection, which will remain permanently at the museum, was assembled over a period of more than 70 years by Captain and Mrs. A. W. F. Fuller of London, in collaboration with Captain Fuller's father, Reverend A. Fuller. Roland W. Force, the museum's curator of Oceanic archaeology and ethnology, spent nearly 6 months in London in daily consultation with Captain Fuller recording on tapes significant data about nearly every one of the specimens. The information is being transcribed and will provide a shelf of reference volumes when completed.

Grants, Fellowships, and Awards

Psychiatry. The Society of Biological Psychiatry is offering an annual award which was made possible by the A. E. Bennett Neuropsychiatric Research Foundation. The award will consist of traveling expenses to the annual meeting plus expenses at the meeting, in addition to an honorarium of $250. It will preferably be given to a youngish investigator, not necessarily a member of the society, for recent work that has not been published. The paper will be read as part of the program of the annual meeting of the society and will appear in the same journal as the other papers read at that meeting. Please submit papers in quadruplicate to Arthur A. Ward, School of Medicine, University of Washington, Seattle 5, Wash., or to Harold E. Himwich, M.D., Chairman, Committee of Award, Galesburg State Research Hospital, Galesburg, Ill. Deadline for manuscripts is *30 April 1959*.

Sterility. The Ortho and Carl G. Hartman grants-in-aid of the American Society for the Study of Sterility, each of $500, are available for 1959. Applications for these two grants should be sent by *31 December* to the secretary of the awards committee of the American Society for the Study of Sterility, Dr. Robert B. Wilson, 200 1st St., SD, Rochester, Minn. No application will be considered by the committee unless it is accompanied by five copies of a brief outline of the research project for which support is being sought.

Scientists in the News

RICHARD G. FOLSOM will be installed as president of Rensselaer Polytechnic Institute in inaugaural ceremonies on 4 October. ROBERT G. SPROUL, president of the University of California for 27 years until his retirement in June, is to make the inaugural address. He is a friend of Folsom, who was associated with the University of California at Berkeley from 1933 to 1953, rising through the faculty in mechanical engineering until he became chairman of the division and director of the mechanical engineering laboratories.

The government of the U.S.S.R. is sending four instrumentation scientists to address the 13th Annual Instrument–Automation Conference and Exhibit sponsored by the Instrument Society of America in Philadelphia 15–19 September. ALEKSANDR M. LETOV, associate director of the U.S.S.R. Institute of Automatics and Telemechanics, will address the opening session on "Instrumentation Education in the U.S.S.R."; BORIS N. NAUMAV, ALEKSANDR M. PETROVSKIY, and ALEKSANDR B. CHELYUSTKIN will be featured speakers at the final-day technical session on "U.S.S.R. Automatic Control."

In addition to Letov, two United States lecturers, NORMAN COUSINS, and GAYLORD P. HARNWELL, will also be featured at the opening session. Cousins, editor of the *Saturday Review* who has been U.S. lecturer to India, Pakistan, Ceylon, and Japan, will relate the role of instrumentation and cybernetics to human progress and world peace. Harnwell, president of the University of Pennsylvania and well-known physicist, will discuss the place of instrumentation in the American university.

HUGH TAYLOR, distinguished chemist and dean emeritus of Princeton University's Graduate School, has been appointed first president of the year-old Woodrow Wilson National Fellowship Foundation. The foundation's main objective is to recruit outstanding students for careers as college teachers. This summer Taylor completed 44 years of continuous service on the Princeton faculty. Immediately after World War II, he supported Whitney J. Oats, chairman of

Princeton's department of classics, in his plans for Princeton's pioneering Wilson fellowship program.

Another Wilson Foundation appointment is that of HANS ROSENHAUPT as the foundation's national director. In accepting his new post, Rosenhaupt relinquished his recent appointment as assistant provost of Columbia University.

In 1957, after the Wilson fellowships had been jointly underwritten for 5 years by 37 American universities and by grants from the Carnegie Corporation and General Education Board, the present program was brought into being with a grant of $24,500,000 from the Ford Foundation for a 5-year period. In its first year of operation the foundation granted fellowships to almost 1000 United States and Canadian students who will enter graduate schools this fall. One of the distinctive features of this recruitment program is that any college faculty member may nominate any eligible student. The Wilson Foundation's new headquarters at 32 Nassau St., Princeton, N.J., were opened on 1 August.

HOWARD BOROUGHS has resigned his position as chief scientist of the Atomic Energy Commission project at the Hawaii Marine Laboratory, University of Hawaii, to join the staff of the Interamerican Institute of Agricultural Sciences, Turrialba, Costa Rica, which has recently started a new laboratory for research and training in the use of radioisotopes in agriculture for Latin American countries.

The National Advisory Committee for Aeronautics has conferred its highest award, the Distinguished Service Medal, on its executive secretary, JOHN F. VICTORY. The award citation reads in part:

"John Francis Victory for almost a half-century has devoted himself unfailingly to the advancement of aeronautics. Since 23 June 1915, when he became its first employee, he has vigorously supported the programs, policies and objectives of the National Advisory Committee for Aeronautics. . . ."

BERNARD M. FRY has been named deputy head of the Office of Scientific Information at the National Science Foundation. Fry joins the foundation from the U.S. Atomic Energy Commission, where he was assistant director for technical information and chief of the AEC Technical Information Service.

W. F. FARAGHER has been appointed assistant to the president of the Temple University Research Institute. The institute, which conducts research in the fields of chemistry at high temperatures produced by combustion or electrical arcs, propellants for missiles, and specialized organic chemistry, plans to extend its work to the petroleum field. For the past 27 years Faragher has been a close associate of Eugene J. Houdry, pioneer in catalytic petroleum cracking processes. Faragher served as director of research, and later as chemical adviser, in the Houdry Process Corporation.

Faragher is a former assistant director of the Mellon Institute, Pittsburgh, Pa. While at the institute, he founded the School of Petroleum Engineering at the University of Pittsburgh, which he headed with professorial rank.

E. YALE DAWSON, formerly associate professor of biology in the Allan Hancock Foundation, has become research director of the newly established Beaudette Foundation for Biological Research at Solvang, Calif. Initial activities of the foundation include studies of the benthic marine botany of the northeastern Pacific.

STEPHEN P. TIMOSHENKO, professor emeritus of Stanford University and a pioneer in the development of engineering mechanics as a science in this country, will receive an Elliott Cresson Medal from the Franklin Institute on 15 October.

ELSA O. KEILES has returned to the Division of Research Grants, National Institutes of Health, as executive secretary of the Metabolism and Nutrition Study Section. For the past 2 years, she has served as professional associate in the Grants and Training Branch of the National Heart Institute.

V. M. INGRAM, member of the Medical Research Council's Molecular Biology Research Unit, Cavendish Laboratory, Cambridge, England, will be a visiting professor in the biology department of the Massachusetts Institute of Technology for a period of 1 year.

JULIAN M. AVERY of Greenwich, Conn., who invented the method of high-pressure operation of blast furnaces for the production of pig iron, will receive the Francis J. Clamer Medal from the Franklin Institute on 15 October.

Recent Deaths

MORTON ARENDT, New York, N.Y.; 81; electrical engineer; assistant professor of electrical engineering at Columbia University, until his retirement in 1943; holder of 50 patents; 22 Aug.

WILLIAM S. AYARS, Leonia, N.J.; 84; retired professor of industrial engineering at Columbia University; had taught at Pratt Institute, Pennsylvania State College, and Nova Scotia Technical College in Halifax; 23 Aug.

WILLIAM H. BRADFORD, Portland, Me.; 92; physician and surgeon; founder and president of the New England Surgical Society; 21 Ang.

ALEXEI M. CHEREMUKHIN, Moscow, U.S.S.R.; 63; leading Soviet aircraft designer; chief deputy of A. N. Tupolev, whose design bureau has produced many of the Soviet Union's most famous aircraft; specialist on stress analysis and tensile strength of materials; 15 Aug.

NEVA R. DEARDORFF, Southampton, N.Y.; 71; associate professor of social economy at the Bryn Mawr College Graduate School; statistical expert in social welfare and health work for more than 40 years; 22 Aug.

EDWARD G. FORD, Kenilworth, N.J.; 53; professor of chemistry at Drew University; 22 Aug.

HENRY F. HELMHOLZ, Rochester, Minn.; 75; head of the pediatrics section of the Mayo Clinic, 1921–46; chief medical consultant for the United Nations Children's Fund in Europe in 1947–48; 19 Aug.

LINVILLE L. HENDREN, Athens, Ga.; 78; professor and head of the physics department at the University of Georgia, 1908–37; dean of the Franklin College of Arts and Sciences, dean of administration, and dean of faculties between 1932 and 1950; 7 May.

ERNEST O. LAWRENCE, Palo Alto, Calif.; 57; director of the Radiation Laboratory at the University of California who made major contributions to the early development of nuclear physics; received the Nobel Prize in 1939 for inventing the cyclotron and last October won the Atomic Energy Commission's $50,000 Fermi Award; recipient of many other national and international honors, including the French Legion of Honor and honorary membership in the Soviet, Swedish, and Irish academies of science; developed the first color television tube; assistant professor of physics at Yale University before joining the University of California in 1928; became a full professor at the age of 29; 27 Aug.

DONALD M. LIDDELL, New York, N.Y.; 79; metallurgist and author of metallurgical and chemical handbooks; 17 Aug.

DANIEL P. O'BRIEN, Torrington, Conn.; 61; administrator of the medical science and research division of the Rockefeller Institute for Medical Research in New York until his retirement in 1947; 16 Aug.

ORMAN C. PERKINS, Brooklyn, N.Y.; 65; neurologist, former professor of neurology at the Long Island College of Medicine and director of neurology for the college's hospital; 14 Aug.

Book Reviews

Loyalty and Security. Employment tests in the United States. Ralph S. Brown, Jr. Yale University Press, New Haven, 1958. xvii + 524 pp. $8.

At least one person out of five in today's 65-million-man U.S. labor force has survived some form of security or loyalty test in his current employment. In what Ralph Brown, professor of law at Yale University, describes as "the security-ridden professions"—some 600,000 scientists, engineers, and public administrators—one out of two (50 percent) is dependent for the opportunity to practice his profession or hold his job on his ability to meet loyalty-security criteria.

Is this bad? Brown's scholarly answer is neither a strident "yes!" nor a complacent "no."

The realities of coexistence with Soviet communism require that we maintain a security system that brings us close to the severities of a garrison state. At the same time we desire to maintain our prized constitutional freedoms and "those human decencies that we prize beyond the Constitution." The search for equilibrium between these competing needs poses problems for statesman, citizen, and professional that have troubled the best minds of our country for more than a decade.

"Our name for problems is significant. We call them headaches. You take a powder and they are gone. These pains . . . are not like that. They are like the pain of earning a living. They will stay with us until death. We have got to understand that all our lives the danger, the uncertainty, the need for alertness, for effort, for discipline will be upon us."

The words are Dean Acheson's; the quotation is a theme of Brown's book. To Acheson's evaluation he makes one significant addition: of equal weight with the need for alertness and discipline is the need to cherish respect for human dignity and individual freedom.

Capitalizing on today's relative calm, which has succeeded the storms of the mid-fifties, Brown applies that sober second thought, which is one of his profession's great contributions to society, to the tangled issues of loyalty and security as they affect employment in all areas of American economic life.

Tests of loyalty, as Brown sees them, are fundamentally tests of disloyalty and, specifically, of "a preference for communism." The attack on disloyalty thus defined has, however, widened in practice to include people who share with communists any preference that to some influential groups seems disloyal, or even politically objectionable. There is room within this formula for attacks on "the whole cloudy constellation of New Dealers, civil libertarians, internationalists, and eggheads." Since disloyalty thus conceived is at bottom a state of mind—as compared to the crime of treason, which requires for conviction proof of an overt act—tests for such a condition require an examination of beliefs.

"The desirable thing to do with loyalty programs is to get rid of them," says Brown—largely, I gather, because of their damping effect on that freedom of thought and expression to which honest opposition ought to be entitled if our democratic, open society is to maintain vitality. Conceding realistically, however, that this prescription is not likely to gain support even in the cooler air of 1958, he recommends at least a retreat to a policy which would require loyalty tests only for federal and state government employees—including public school teachers, members of the bar, and officers and staff members of labor unions. That such would be a retreat may surprise some readers, who have not heard that boxers and wrestlers, before they can appear in Indiana, must subscribe to a loyalty oath.

Security programs, by contrast, Brown sees as essential. To some extent security programs and loyalty programs cover the same field since judgments about past, present, and future disloyal conduct are part of the decision that a particular individual will conduct himself in the future in a way significantly harmful to a substantial national interest. Thus Brown concedes that, even if loyalty programs as such were abandoned, the thorny problems raised in any examination of beliefs would plague us still. They would be ameliorated, however, he argues, by putting them in the focus of a narrower question: Is this person one who *may* —with more than average probability —injure the nation? And he would sharply reduce the numbers involved by restricting security tests to employment in sensitive positions: those in which the holders could substantially injure national security.

To confine the excesses of loyalty employment tests within reasonable bounds, Brown sees it as essential that the accused employee be entitled to all of the procedural elements of a fair trial, including specific charges, an opportunity to confront those on whose testimony reliance is being placed, a fair hearing, a reasoned decision based on the record, and an opportunity for review of arbitrary decisions. For security programs, Brown recognizes that the analogy to decisions about suitability for employment generally is controlling and that due process must be measured by less rigorous standards: "the question is essentially the confidence of one man in another." Security programs are tolerable if their coverage is reduced, if standards and criteria are revised to emphasize "the whole man," if security officers are kept in an advisory role, and if hardship is minimized by "a forceful policy of providing other jobs for those who are excluded from security-sensitive positions."

Perhaps the most important parts of this book are not its conclusions but the material it collects, organizes, and presents and the care with which its analyses are reasoned. Its encyclopedic coverage and scholarly footnotes provide a wealth of guidance for those who must suffer the headaches in this troubling area of our national life, whether as security officers, counsel, board members, judges, legislators, executives or citizens. Its penetrating and exhaustive examination of every relevant facet and significant incident—loyalty tests in unclassified research, the employment policies of universities, the impact of security and loyalty on scientists and engineers, and many others—insures that it will have a permanent place in the literature of our political science. Its moderate and balanced tone makes it a guide to equity and reason in a field where both are all too rare.

WILLIAM A. W. KREBS
Arthur D. Little, Inc.,
Cambridge, Massachusetts

Matter, Earth, and Sky. George Gamow. Prentice-Hall, Englewood Cliffs, N.J., 1958. xiii + 593 pp. Illus. $10.

George Gamow is deservedly acclaimed one of the foremost interpretive writers in the field of science today. A number of his books and articles have been translated into as many as 16 languages, and he was awarded the Kalinga prize by UNESCO (1956) for his popularization of science. His success stems not only from the zest with which he

relishes and presents his material but also from his skill in weaving the principles and concepts of science into a pattern which is both meaningful and strikingly his own.

Gamow has repeatedly proved to be readable, and his latest book is no exception; it is a gay and exciting excursion into the physical sciences. The approach is a refreshing one. The book is written in the form of a trilogy, dealing first with things of our own size, second with the microcosmic world, and finally with the macrocosm. This departure from the usual historical approach allows a more continuous presentation of physics, chemistry, astronomy, and geology and will be appreciated by the general reader. It is evident that considerable effort and thought have been given to the problems of conjoining the contents of each section into a whole (this is most successfully accomplished in the macrocosmic section) and of keying the more difficult concepts of modern science to the simple level of presentation used in the first section. As an aid to the assimilation of the material, the author has included many entertaining illustrations and photographs.

The volume appears to be written for the general reader, but the addition of questions and answers and the publisher's advertisement, as well, suggest that it may be intended as an introductory text for nonscience students. For this purpose the book is probably oversimplified, and the amusing style tends to obscure the drama of science. However, the general reader will be handsomely rewarded, for he will find the author to be an illuminating writer on scientific matters as well as a provocative prophet. Says Gamow, "To sum up, we can say that the state of physical sciences today can be compared with the state of geography a few centuries ago: there are no Americas to be discovered any more."

W. P. BINNIE

Department of Physics,
Purdue University

The Measurement of Colour. W. D. Wright. Macmillan, New York, ed. 2, 1958. ix + 263 pp. Illus. $10.75.

Since 1931, when the Commission International de l'Eclairage (CIE) adopted the Standard Observer System for Colorimetry, color measurement and specification have grown tremendously. Wright's efforts in the development of this system eminently qualify him to write a book on the measurement of color. Although the book treats this specialized field from the psychophysicist's viewpoint, it is written in language that nonspecialists can fully comprehend.

Wright develops the story of tristimulus colorimetry in a logical and informative manner. The first two chapters treat the physical and physiological concepts of visible radiation. The next two chapters present the principles underlying photometry and colorimetry, culminating in the definition of the 1931 CIE standard observer. Chapters 6 and 7 describe the means by which color may be measured (colorimeters and spectrophotometers) and by which colors may be specified and represented (color spacings and color atlases). The final two chapters discuss such important applications of the system as color photography, color printing, and color television and give a behind-the-scenes view of the reasons forcing consideration of revision of the system, ending with the open-minded statement that only the future will show whether the data currently being gathered will "justify a revision of the standard observer data."

There are, regrettably, several prominent inadequacies: nonphysical use of the term *power* to describe "capability"; incomplete captioning of figures for the spectral distribution curves of sources, so that the tyro may draw erroneous conclusions regarding the energy in these sources; and reversal on plate 4 of the bottom and top colors printed to represent effects of decreasing saturation on the spectral reflectance curves of pigments. On the whole, however, Wright has prepared an excellent revision of his earlier work (1944). He does not presume to be an oracle who answers all color-measurement problems, but rather presents the reader a clear insight into the CIE Standard Observer System.

I. NIMEROFF

Optics and Metrology Division,
National Bureau of Standards

Proceedings of the Second International Congress of Surface Activity. vol. I, *Gas/Liquid and Liquid/Liquid Interface,* 521 pp., $15; vol. II, *Solid/Gas Interface,* 348 pp., $12.60; vol. III, *Electron Phenomena and Solid/Liquid Interface,* 621 pp., $16.80; vol. IV, *Solid/Liquid Interface (Washings, Etc.) and Cell/Water Interface,* 352 pp., $12.60. J. H. Schulman, Ed. Academic Press, New York; Butterworths, London, 1957. $50 per set.

These four volumes contain the papers presented at the second International Congress of Surface Activity, held in London in the spring of 1957. The amount of material contained in the four volumes is very great and reflects the outstanding success with which the efforts of the organizers (Schulman and his school) have been so justly crowned. The speed with which the work has been published reflects credit on publisher and authors alike, for this is no small achievement.

Since the list of contributors and titles is so long, I feel that to select just a few names would be unjust, but the truly international character of the meeting may be briefly indicated by such names as Ekwall (Finland), Derjaguin and Trapeznikov (U.S.S.R.), de Boer and Overbeek (Holland), Nilsen (Sweden), Sata and Sasaki (Japan), and Alexander (Australia).

The topics of the four main activities of the meeting are conveniently grouped in individual volumes. Volume I deals with general adsorption problems at the gas-liquid and liquid-liquid interfaces, as well as with applications of these studies to typical systems of practical interest—for example, evaporation from water reservoirs, solubilization in detergent solutions, and emulsification. Volume II deals exclusively with adsorption on solid surfaces, one section comprising physical adsorption—particularly with reference to heat of adsorption—and the other section dealing with an interesting variety of problems in chemisorption. Volume III deals with electrical phenomena at the mercury-water and other interfaces, and with such aspects of the solid-liquid interface as flotation and adsorption, while volume IV is concerned with other aspects of the solid-liquid interface, such as problems in detergency, as well as with the surface chemistry of cell and tissue interfaces. The last two volumes illustrate very well the increase which has occurred in recent years in the state of knowledge relating to such apparently diverse phenomena as the flotation of minerals and biological surface chemistry.

These books represent more than simply a collection of (for the most part) admirably brief but well-documented papers dealing with specific items in surface chemistry. Following the excellent precedent set by the Faraday Society, the organizers of the congress allowed time for discussion of the papers, and the keen discussions are reproduced along with the papers. The discussions seem to me to be a valuable feature; they aid the reader in evaluating the occasionally rather strongly worded claims in certain of the papers, and they contribute towards bringing the material into a more coherent whole. Would that more meetings were run along these lines!

Although, to be sure, the many contributions deal with individual items, even the general reader can gain sight of a good cross section of current activity in surface chemistry from these four volumes, and it is heartening to see such breadth of study represented here. Specialists will be more concerned with individual volumes; thus, solution-chemists will find more in volume I than elsewhere, and workers in the field of cata-

Kodak reports on:

the rose arbor, the finch, or the chondrosarcoma in color on paper . . . a ceramic magnet, a coil, a capacitor, a germanium diode, and some nylon bearings...an organic too versatile to lie down and die

Be creative, if you insist

Persons who deplore photography as mechanistic submergence of the human spirit may, if they wish, go on sketching anatomical specimens with a charcoal pencil and then retire to the library to enjoy their personal collections of authenticated original Botticellis. But here's the dope on the new *Kodacolor 135 Film* for miniature cameras—in case you prefer photography. It is the first Kodak color film expressly made for obtaining color prints with a 35mm camera.

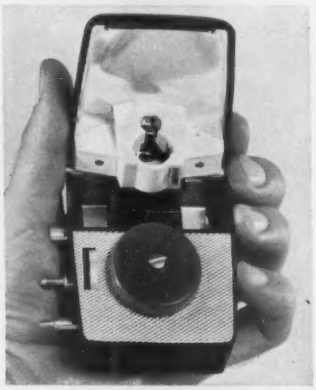
You bring your exposed film to your dealer. He sends it to a color processor—of which gentry Kodak is one. Kodak provides 2½ x 3½-inch enlargements (2X from the 35mm negative) at 23¢ each list, or 3½ x 5's (3X) at 32¢ list. To compensate for numerous unknowns along the way, we have to exercise (electronically) for each negative an individual judgment of the color balance you would like. By dint of intensive studies employing techniques of experimental psychology and statistical analysis and by further dint of having made quite a pile of satisfactory prints already, we generally hit it right.

If your subject is a rare tropical finch or a chondrosarcoma instead of someone's blond granddaughter in front of a rose arbor and you're going to a color lab for a custom job, it wouldn't be a bad idea to include a neutral grey card outside the area of interest in the original picture. If you ask to have the grey card rendered as grey and then cropped off, no color processor can go far off faithful color rendition of your subject.

You have an alternative to color lab processing, of course. For 75¢ a Kodak dealer will sell you a copy of the brand new Kodak Data Book, "Printing Color Negatives." You can study that and then make your own prints and your own decisions, using the right Kodak chemicals and *Kodak Ektacolor Paper* (formerly called Kodak Color Print Material, Type C).

Try it. During that first night in the darkroom the human spirit will find plenty to keep it occupied.

4 twirls for 1/5 joule



Here is a new Kodak device, obtainable for only $13.95 (list). It converts a twirl of your fingers into a half-million-erg jolt of d-c energy, four twirls for 200 watt-milliseconds. With a thousand ohms of load resistance, 63% of the four twirlsworth of energy is discharged within 150 milliseconds, in a surge that starts at 50 volts. The energy can be taken off from the socket in the hinged cover. To trip, you close circuit between the projecting screw at the left and the lower stud, first having wedged the knurled nut firmly to the left in its slot.

Don't complain that the device could be designed for better mechanical convenience. We are merely trying to be helpful. For commercial practicability, we have had to design the *Kodak Generator Flasholder* to the convenience of those who want to snap it onto a camera —almost any camera—for photoflash pictures that will never miss synchronization because of aged batteries.

For your part, you ought to be willing to put in a few minutes of junkbox-inspired inventiveness in adapting the gimmick to your own high scientific purpose. There is no need to write, wire, or phone. Just march down to the nearest camera counter.

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Is $3 too much to ask for one gram of *Toluene-3,4-dithiol* (Eastman 4508)? We'll tell you why we ask.

In 1937, within a year after a British chemist announced that this compound is a reagent for tin and nicknamed it "dithiol," we tried to make some. Our luck was poor. Yield was 8%, and quality was dubious. We decided to forget about it.

Yet dithiol refused to lie down and die. Chemists have persisted in writing papers about it—"most promising colorimetric reagent for tin"; molybdenum determination in soils, metals, and rocks; precipitant for metals of the H_2S group; simultaneous determination of molybdenum and tungsten in biological materials; the zinc-dithiol complex as a reagent for arsenic and germanium; semi-microanalysis for bismuth; and on and on. There was a market there, all right.

Once we came close to doing something about it. A paper in the Indian literature, though it discussed another compound, struck us as offering a sound route to dithiol. We talked ourselves out of trying it on the grounds that dithiol had a short shelf life.

Eight more years slipped by before the break came. An inquirer so goaded us with his scoffing at our pessimism about dithiol and with his taunt about what a cinch it was that we lost our head a little and bought the right to use his method. We don't react that way very often.

His method seems to have worked. We find ourselves in possession of a large stock bottle full of dithiol. Over the dithiol there is nitrogen, just to be surer. It is to be hoped that all who have inquired about dithiol over the past 21 years are still alive and well and interested in analytical chemistry.

Procedural abstracts on the more promising applications of dithiol are obtainable without charge from Distillation Products Industries, Rochester 3, N. Y. (Division of Eastman Kodak Company). Likewise obtainable is the new List No. 41 of some 3700 Eastman Organic Chemicals, out of which, happily, dithiol is but one.

Prices stated are subject to change without notice.

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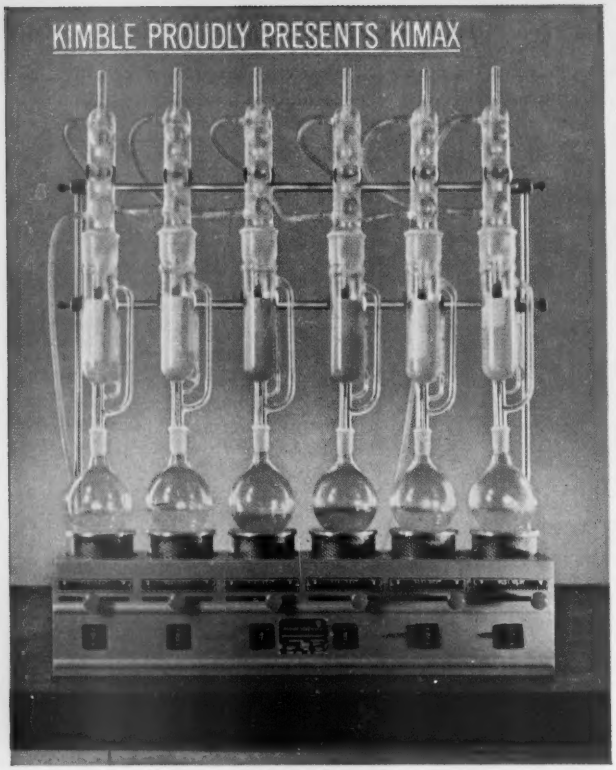

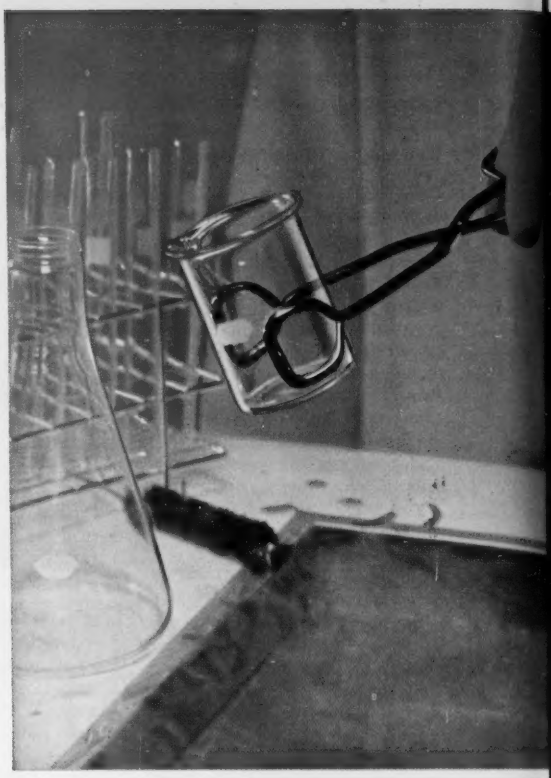

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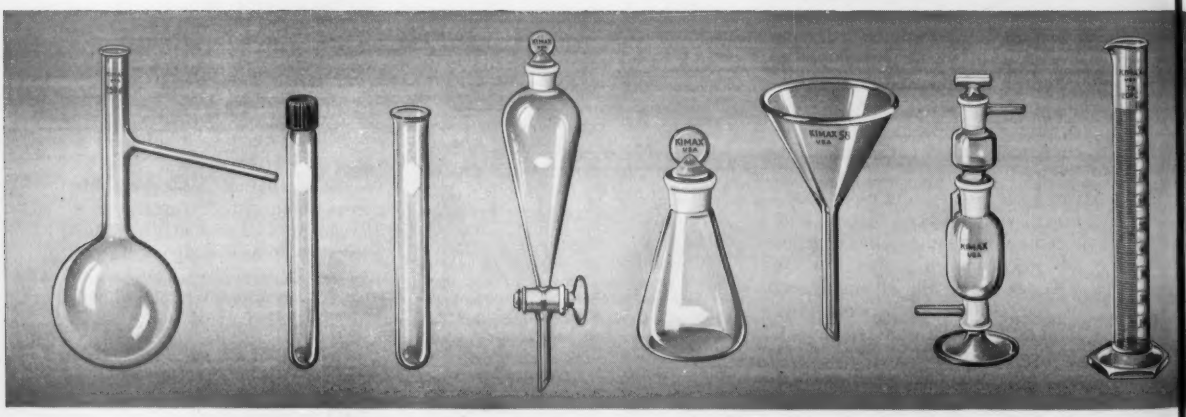

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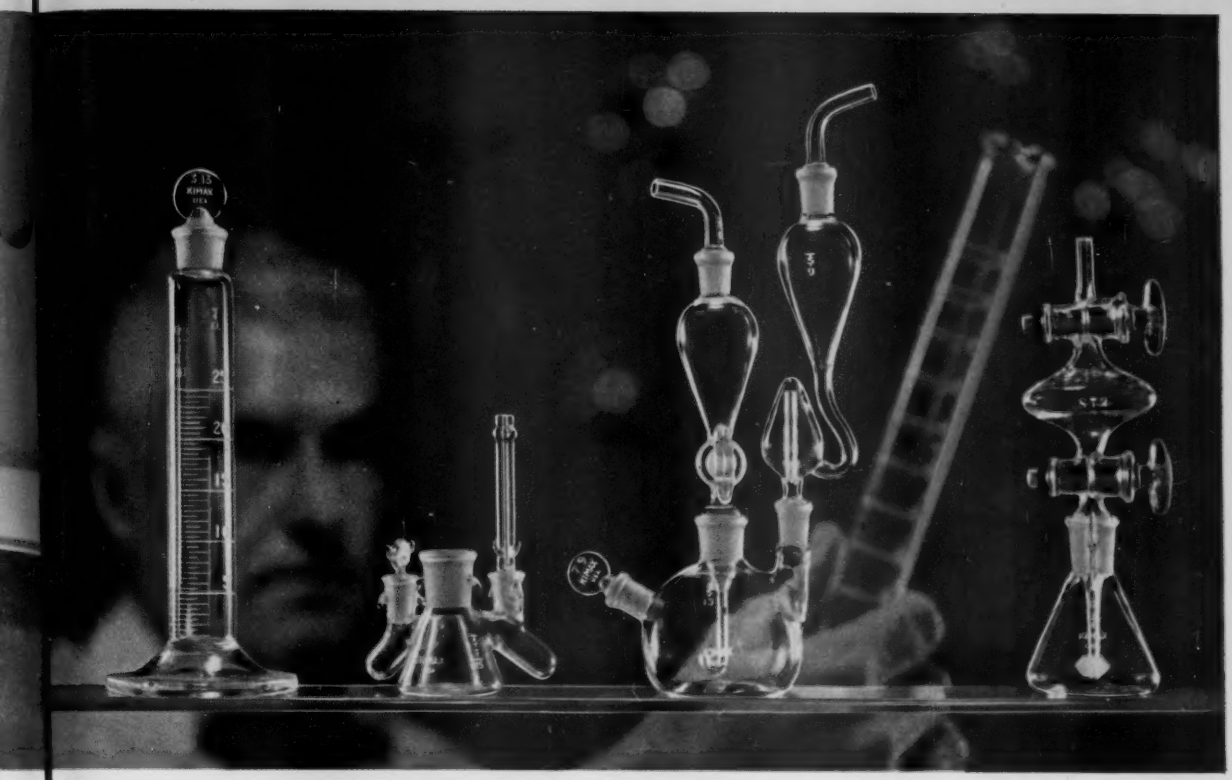

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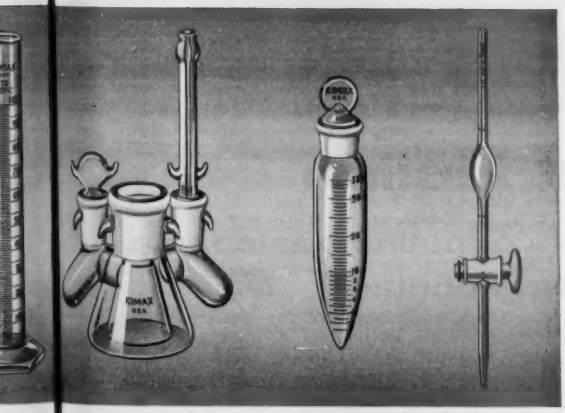

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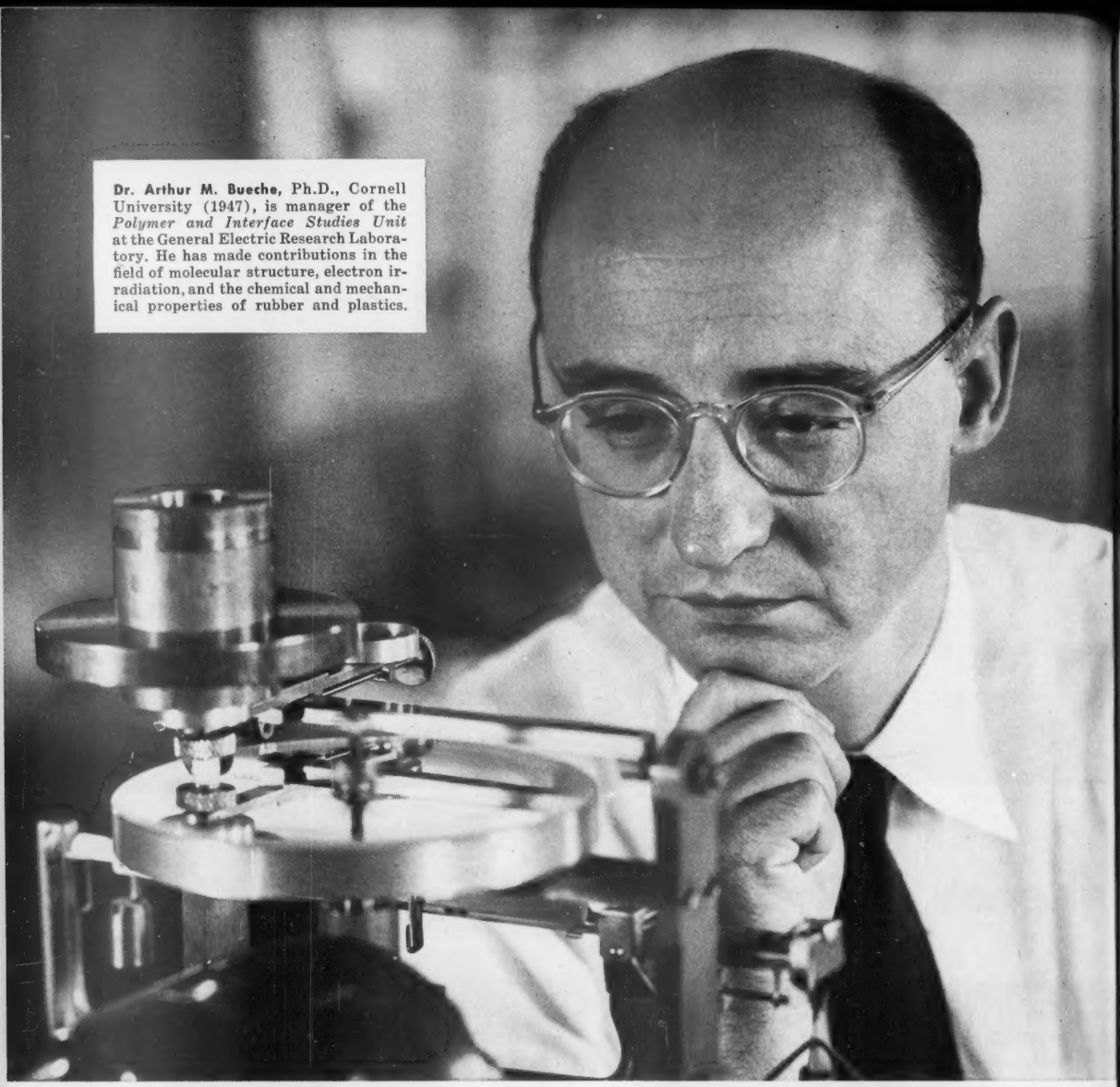

Dr. Arthur M. Bueche, Ph.D., Cornell University (1947), is manager of the *Polymer and Interface Studies Unit* at the General Electric Research Laboratory. He has made contributions in the field of molecular structure, electron irradiation, and the chemical and mechanical properties of rubber and plastics.

A deep look at friction

General Electric's Dr. A. M. Bueche explains basic facts about materials in moving contact

Scientists recently have observed substantial differences in the rolling speed of steel balls on materials that have essentially identical surfaces but are dissimilar in their internal structure. Thus *friction,* which usually has been considered to be purely a *surface phenomenon,* is now known to be dependent also on the *bulk mechanical properties* observed "beneath the surface" of the materials involved.

Dr. Arthur M. Bueche and his associates at the General Electric Research Laboratory have developed new fundamental theories explaining these surprising friction effects. Their work, which also includes basic studies in surface chemistry, is giving new insight into a problem that has harassed designers and engineers ever since men first began making machines with moving parts.

Imaginative research programs, like these led by Dr. Bueche, are making progress toward new and improved products that will not only help raise our level of living, but also will contribute to a stronger defense for the nation.

Progress Is Our Most Important Product

GENERAL ELECTRIC

lysis will be predominantly interested in volume II, whereas those concerned with mineral processing and flotation will find their subject covered in volume III. Although the subject of biological surface chemistry is recorded in only a limited number of papers in volume IV, biologists will find these profitable reading.

The standards of printing, format, and binding are high. Errors are few, and though the editor attributes the success of the publication to his many contributors, one cannot help thinking that this is overmodesty on his part. The price for all four volumes is high, but justified, and for those readers concerned with only one or two areas of study, the volumes are available singly.

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Department of Chemistry,
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Physique électronique des gaz et des solides. Michel Bayet. Masson, Paris, 1958. 246 pp. Illus. F. 4900.

This book is based on material taught in a course by the author at the Faculté des Sciences de Toulouse for candidates for the "electronics certificate"; the course material is augmented by a number of theoretical developments, which are in part original. The purpose of the book is to give a unified account of transport phenomena associated with the motion of electrons in gases and solids; the greater part of the book (174 pages) deals with gases, the remainder being devoted to metals and semiconductors.

In the first chapter, the author briefly reminds the reader of the elements of Boltzmann, Fermi-Dirac, and Bose-Einstein statistics; the second part of this chapter discusses the classical theory of collisions between two particles. Chapter 2 deals with the kinetic theory of gases; the Boltzmann transport equation, diffusion, viscosity, thermal conductivity, and so on are discussed along standard lines.

In chapter 3 the author gives a detailed mathematical discussion of the transport properties of a nondegenerate Lorentz gas—that is, of a mixture of two gases, A and B, in which the A-A interaction is negligible compared with the A-B and B-B interactions. The results obtained in this chapter are carried over to the next one, in which the electromagnetic properties of a plasma are investigated. In chapter 5 one finds a rather standard treatment of the fundamental processes in ionized gases, such as ionization, excitation, and recombination. The various types of gas discharges are considered in chapter 6, which constitutes the last chapter dealing with gases. The last two chapters deal with the electron theory of metals and semiconductors. The appendix contains mathematical details of derivations and gives properties of certain mathematical functions used in the text.

The general level of this book corresponds to senior undergraduate or beginning graduate physics courses in this country. It is clearly written and should serve a useful purpose for those who are interested in electron physics—particularly, of gases. The publishers should be congratulated on the good general appearance of this book.

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Department of Electrical Engineering,
University of Minnesota

The Origins of Modern Science, 1300–1800. H. Butterfield. Macmillan, New York, ed. 2, 1957. x + 242 pp. $3.

In the eight years since the first edition of Butterfield's worthy *Origins* appeared on the market, perhaps no single volume has been so widely used in introductory courses dealing with one or another aspect of the scientific revolution. This is surely proof positive of its basic correctness and balance as well as of its extreme readability, for which its author, master of Peterhouse in the University of Cambridge, has come to be justly praised. Perhaps no better indication can be found of the popularity of this relatively slight book as well as the esteem in which it is held than the fact that one repeatedly hears professional historians of science express two desires: (i) that comparable studies suitable for textbook purposes existed for other periods in the history of science, and (ii) that *they themselves* had written this particular book.

In view of such kudos, it is slight wonder that its author and publisher should wish to perfect it by correcting any noted errors or misprints, by adding relevant material to the existing chapters of the original structure, and by keeping it up to date through the addition and use of entries under "Suggestions for further reading." The result is a revised edition, some 55 pages longer than the first edition, as eminently sound as ever, and no doubt headed for even greater success.

While the general content and number of the original chapters remain unchanged, I note the following additions. Pages 34–36 add useful ideas concerning ancient, nonscientific elements in Renaissance thought—including the role of occultism and cabalistic speculation—which help to round out the chapter on "The conservatism of Copernicus." This brilliant chapter, supporting the view that Copernicus' work can more meaningfully be viewed as the end of the old astronomy and cosmology than as the beginning of the new, still, however, contains a possibly misleading concept. Of Copernicus we read, "To the old objection that if the earth rotated its parts would fly away and it would whirl itself into pieces, he gave an unsatisfactory answer. . . ." (page 32). Coupled with the allusion to Ptolemy on the following page, the reader could well get the erroneous impression that Ptolemy had faced "that whole question of centrifugal force." However, Ptolemy nowhere argues in such terms, or indeed says anything about what would happen if the earth were to rotate upon its axis. The truth of the matter is that Copernicus in *De revolutionibus* (book I, chapters 7–8) erroneously ascribed such an argument to Ptolemy and, unfortunately, most modern scholars writing about Copernicus have not bothered to check by reading Ptolemy.

Other material new to this book includes a section dealing with the work of Duhem and others on the theory of impetus (pages 14–16) and a section on the communications of scientists and early scientific societies in the 17th century (pages 71–76). Additional suggestions for further reading include such important work as T. S. Kuhn's paper on "Robert Boyle and structural chemistry in the seventeenth century" and E. Rosen's *Three Copernican Treatises.*

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Department of Humanities,
Massachusetts Institute of Technology

Elements of Water Supply and Waste-Water Disposal. Gordon Maskew Fair and John Charles Geyer. Wiley, New York; Chapman & Hall, London, 1958. vii + 615 pp. Illus. + chart. $8.95.

Conventionally and traditionally the undergraduate student of civil engineering has been introduced first to the subject of municipal water supply and treatment, then later to a separate and largely unrelated course in sewerage and sewage disposal. Yet the basic disciplines and engineering sciences governing all aspects of water supply and waste-water disposal are similar, whether the water passes through municipal, industrial, or agricultural systems. Although chemical engineers have long recognized these mutualities by stressing "unit processes and unit operations" that are applicable to many industries, Fair and Geyer have pioneered in utilizing this approach for sanitary engineering. Sedimentation and flotation, for example, involve identical principles of fluid mechanics whether they are used for water treatment, sewage clarification, or the separation of solids and oils from industrial wastes. Fair and Geyer emphasize the similarities of the fundamental principles and then go

on to describe the application to special situations.

Their original unabridged text, *Water Supply and Waste-Water Disposal* (Wiley, 1954), was a thorough treatise that stressed the application of scientific principles, rather than conventional practice, to the functional design and operation of water works and liquid-waste facilities. The new volume is a condensed version of the original text, with some subject matter simplified, some recast, and some shortened. A new feature of the present volume is the collection of 175 problems at the end of the book. Together with abundant examples that serve to illustrate and demonstrate scientific principles and formulas, these problems enhance the utility of the new volume as a textbook. The numerous illustrations and graphs are simple line sketches, uncluttered by details. Photographs are not used.

This book, like most other writings by these authors, is characterized by rigid organization, careful documentation, exemplary grammar, and a meticulous selection of words. It is designed for careful and prolonged study, not for casual perusal or for occasional reference. In company with its larger prototype, it is the most fundamental and rational treatise available in the broad field of water supply and waste-water disposal.

J. E. McKee

Division of Engineering,
California Institute of Technology

Miscellaneous Publications

(Inquiries concerning these publications should be addressed, not to Science, *but to the publisher or agency sponsoring the publication.)*

Bentley and Driver's Qualitative Chemical Analysis. Revised by J. E. Driver. Hong Kong Univ. Press; Oxford Univ. Press, New York, rev. ed. 5, 1958. 47 pp. $1.20.

Smithsonian Contributions to Astrophysics. vol. 2, No. 9, *On Two Parameters Used in the Physical Theory of Meteors.* Luigi G. Jacchia. Smithsonian Institution, Washington, 1958 (order from GPO, Supt. of Documents, Washington 25), 8 pp. $0.15.

Skin Resistance Changes during Acceleration. WADC Tech. Note 56–397. ASTIA Document No. AD 97 275. Sanford I. Cohen, Albert J. Silverman, George D. Zuidema, Gilbert E. Johnson. Wright Air Development Center, Wright-Patterson Air Force Base, Ohio, 1958. 13 pp.

Research Bulletin of the Panjab University. Zoology, No. 116; *Studies in Reptilian Spermatogenesis*; No. 3, *Spermatogenesis of the Spiny-Tailed Lizard,* Uromastix hardwickii *Gray, with Observations on the Living Material under the Phase-Contrast Microscope*; Bhupinder Nath Sud; 16 pp.; Rs. 2/59. Chemistry, No. 117; *Fat Formation from Different Carbohydrates by* Penicillium Aurantiobrunneum *and the Effects of Varying* pH, *and Nitrogen Sources on the Production of Fat from Sucrose*; Jagjit Singh and Gurmit Singh; 34 pp.; Rs. 0/85. Zoology, No. 118; *The Cytoplasmic Inclusions of the Neurones of the Earthworm*; S. K. Malhotra; 14 pp.; Rs. 2/39. Zoology, No. 119; *On the Direct Origin of the Refringent Granules from the Golgi Spheroids in the Spermatogenesis of the Nematodes,* Polydelphis *Sp.*; Sant Singh; 6 pp.; Rs. 1/39. Zoology, No. 120; *Cytological Studies on the Indian Spiders.* G. P. Sharma and Sant Singh. 5 pp.; Rs. 1/19. Zoology, No. 121; *Studies on Insect Spermatogenesis*; No. 3, *Odonata: Spermatogenesis of* Neurobasis *sp.*; Sukhdev Raj Bawa; 5 pp.; Rs. 1/17. Zoology, No. 122; *Cytological Studies in Heteroptera*; No. 3, *A Comparative Study of the Chromosomes in the Male Germ-Cell of Eleven Species of the Sub-Family Pentatominae*; Ram Parshad; 20 pp.; Rs. 2/75. Zoology, No. 123; *A Study of the Cytoplasmic Inclusions of the Neurones of the Snail,* Euaustenia, *by Phase-Contrast Microscopy and Sudan Black Colouring*; S. K. Malhotra; 5 pp.; Rs. 1/27. Mathematics, No. 124; *Certain Averages Connected with Partitions;* Hansraj Gupta; 4 pp; Rs. 1/03. Botany, No. 125; *The Polyporaceae of the Mussoorie Hills, II.* K. S. Thind and M. S. Chatrath; 12 pp.; Rs. 2/30. Zoology, No. 126; *Fish Spermatogenesis with Particular Reference to the Fate of the Cytoplasmic Inclusions*; No. 4, *Spermatogenesis of* Ophiocephalus punctatus; Hem Sagar Vasisht; 4 pp.; Rs. 1/06. Mathematics, No. 127; *Spheres Associated with a Semi-Orthocentric Tetrahedron*; Sahib Ram Mandan; 5 pp.; Rs. 0/95. Zoology, No. 128; *Some Observations on the Biology and Oviposition of* Bruchus Analis *F. (Bruchidae: Coleoptera)*; G. L. Arora and H. R. Pajni; 18 pp.; Rs. 3/00. Botany, No. 129; *The Polyporaceae of the Mussoorie Hills, III*; K. S. Thind, P. S. Bindra, M. S. Chatrath; 13 pp.; Rs. 2/36. Zoology, No. 130; *Some Observations on the Biology of* Lipeurus Tropicalis *Peters (Mallophaga: Ischnocera)*; G. L. Arora and Narinder Perkash Chopra; 7 pp.; Rs. 1/47. Panjab Univ., Hoshiarpur (Panjab, India), 1958.

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Reports

Detection and Titration of Asian Influenza A Virus by HeLa Cell and Monkey Kidney Cell Cultures

Vogel and Shelokov (*1*) have described a method whereby the presence of influenza virus may be detected with relative ease in monkey kidney cell monolayer cultures. Influenza virus was first adsorbed on monkey kidney monolayers, and later guinea pig erythrocytes were agglutinated on the infected cell sheet. In this manner visual evidence of infection was elicited. Our studies have confirmed these results, and the method has been extended to include the quantitative titration of influenza virus and the use of HeLa cell cultures for both detection and titration. A comparison of this method of titration with the classical hemagglutination (HA) titration suggests that the new method is many times more sensitive than the hemagglutination tests.

Five-day-old primary cultures of monkey kidney cells prepared by the method of Youngner (*2*) and grown in medium M202 (*3*) with 2 percent rabbit serum were used throughout the experiments.

Eight-day-old monolayer cultures of cell strain HeLa (Gey) completely adapted to growth on rabbit serum supplemented medium were used in these experiments in either T-9 flasks or screw-cap tubes. The HeLa cells were grown in a routine medium consisting of 15 percent rabbit serum and Scherer's maintenance solution MS (*4*).

The strain of influenza A used had been isolated locally in eggs and was identified as Asian type. It had been designated A/NS/45/57, and the current stock after five amniotic passages in 10-day-old embryonated eggs had a hemagglutination titer by the method of Salk (*5*) of 80 HA units per milliliter. This HA titer was checked frequently throughout the experimental period so that a comparison could be made of the sensitivity of titration methods. All dilutions of A/NS/45/57 were made in the same diluent, Scherer's MS with 5 percent rabbit serum, whether the cells to be infected were monkey kidney or HeLa.

Monkey kidney or HeLa cell monolayers were infected with serial half $\log_{10}$ dilutions of stock (80 HA units per milliliter) influenza virus A/NS/45/57. Three screw-cap tubes or T-9 flask cultures were infected at each dilution of virus. The infected cultures and uninfected controls were then incubated at 37°C for 48 hours.

After incubation the cultures were washed twice with phosphate-buffered saline (*6*), and 1.0 ml of a 1 percent suspension of fresh chicken erythrocytes in phosphate-buffered saline was pipetted into the culture flask. This suspension was allowed to remain over the cell sheet for 5 minutes, during which time the erythrocytes sedimented onto the monolayer. After 5 minutes the cultures were again washed gently twice in phosphate-buffered saline and stained.

The washed cell sheets, either HeLa or monkey kidney cells, were first dried and fixed for 1 minute in purified methanol and then stained for 5 minutes with 0.15 percent Leishman's stain in acetone-free methanol. The preparation was then washed twice with distilled water and allowed to stand for 10 minutes before observations were made.

Preparations were examined at a magnification of 60 with a microscope, the eyepiece of which had been adapted so that the field was square and bisected by grid lines into four smaller squares. The clumps of agglutinated erythrocytes had stained pale pink and contrasted with the pale blue cell background.

During the counting procedure all cultures were selected and numbered at random, and the operator was unaware of dilution values. Figure 1 shows the results obtained with both HeLa and monkey kidney cell cultures. In this figure each point is the average of six field counts and two separate experiments (three field counts at each dilution per experiment). The results show that a straight line gives a reasonable fit to the data plotted as the number of clumps versus dilution of virus. It can also be appreciated from Fig. 1 that the amount of virus which can be detected by the titration method corresponds to roughly 0.08 HA units of virus.

In order to test the specificity of this clumping reaction, use was made of various types of influenza antisera. The antisera, in threefold dilution, were placed over the infected and control HeLa cell monolayer cultures for 1 hour before the cultures were processed as described above for clump counting. Neither B-Lee, FMI nor A-Can (A-prime strain) antisera reduced the ability of infected cell sheets to agglutinate and clump erythrocytes. However, a hamster antiserum specific for Asian influenza A virus prevented clumping up to a dilution of 1:90.

During a recent influenza epidemic sputum specimens were collected from suspected cases and processed by classical embryonated egg isolation methods for the isolation of influenza virus. Some of the sputum specimens from which influenza virus type A (Asian) was isolated were used to infect monkey kidney and HeLa cell monolayers. One milliliter of these specimens, in 3 percent tryptose phosphate broth, was placed on the cell sheet and incubated at 37°C for 1 hour. The sputum specimen was then removed and replaced with 5 percent rabbit serum in Scherer's MS. Cultures thus treated were then incubated again for 72 hours and processed for clump counting as indicated above.

With HeLa cells, six out of seven egg-positive specimens were also considered positive by the adsorption hemagglutination method. A specimen was considered positive if at least five well defined clumps of chicken erythrocytes could be counted on a routine screw-cap tube monolayer culture. With monkey kidney cells, it was considered that all five specimens out of five processed were positive.

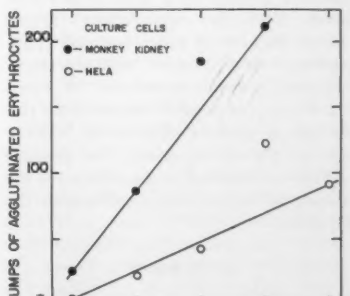

Fig. 1. Titration of influenza virus A/NS/45/57 by clump counting.

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper. (Since this requirement has only recently gone into effect, not all reports that are now being published as yet observe it.)

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

This method of detecting influenza virus may be of use where tissue-culture methods are deemed more suitable than isolation by means of the embryonated egg. However, we wish to point out that the egg isolation method has been found by us to be many times more sensitive. The stock virus A/NS/45/57, containing 80 HA units per milliliter and with an end-point titration by the adsorption-hemagglutination method of about $10^{-3.1}$, has an egg infective dose 5 percent of close to 10^{-8}.

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16 April 1958

Instantaneous Linear Velocity of Flow in Pulmonary Artery Measured by a Catheter Tip Method

Abstract. Measurements of the instantaneous linear velocity of blood flow in the pulmonary artery of the human have not been reported previously. This report describes a catheter tip method for making such measurements.

A double-lumen catheter was designed (*1*) with one opening in the tip and the other 4 mm from the tip on the side of the catheter. When the catheter is positioned in the pulmonary artery, the pressure recorded from the tip is less than that from the side opening, because of the "drag" of the blood flowing past the tip. Accordingly, in this method, the catheter is used as a Pitot tube facing away from the approaching stream rather than into it as in the usual application of the Pitot tube. With the use of standard pressure transducers of equal sensitivity it is possible to record the difference in pressure which exists between the tip and side openings. The pressure difference is related to the velocity of the stream at the tip of the catheter by the equation

$$v = c(2g\Delta p)^{1/2}$$

where v is the velocity, g the gravitational constant, Δp the recorded pressure difference, and c a constant, all expressed in consistent units. The value of c, 0.3 for forward flow, was determined by repeated, reproducible measurements of Δp with the catheter in a long straight tube through which water was forced at different, known rates of flow. The catheter in this, and in other studies made with pulsatile flow, tended to seek the axis of the tube and showed a minimum of vibratory motion or "whip." Nor was significant whip noted in the measurements in the pulmonary artery reported here. For retrograde flow, a value of 0.8 was assumed for c.

In Fig 1 are shown the almost superimposed pressure tracings from the two lumina of the catheter, obtained in the pulmonary artery of an adult. The zero point of the pressure curve from the tip was arbitrarily displaced slightly above that of the pressure curve from the side opening so that the pressure tracing from the tip lies below that from the side opening only during periods of rapid forward flow, when the tip pressure was so reduced by the "drag" as to offset the displacement of the zero point. The pressures were recorded at two points, one close to the pulmonic valve, the other in a major branch of the right pulmonary artery, well distal to the valve. Shown below the pressure tracings in Fig. 1 are the corresponding curves of the difference in pressure between the tip and side openings.

The pressure tracings recorded from the two sites in the pulmonary artery are technically satisfactory. Aside from slight differences in the systolic and diastolic pressures, they differ chiefly in that the dicrotic notch and the succeeding rise in pressure occur later in the tracings from the distal position. The differential pressure curves differ in several respects. Close to the valve, there is a rapid increase in the velocity of ejection immediately following the onset of systole. The maximum velocity (29 cm/sec) occurs just prior to the pressure maximum; the velocity then decreases rapidly to zero. The entire period of forward flow lasts 0.2 sec and ends just before the appearance of the dicrotic notch. There follows a period of backward flow lasting just over 0.1 sec and ending with the completion of the dicrotic notch. It is succeeded by a short period of lesser forward flow, which, in turn, is followed by two or three small oscillations before the start of the next ejection. The duration and timing of the backward flow suggest that it is associated with the retrograde movement and closure of the semilunar cusps.

These curves differ from the only other published curves of instantaneous velocity in the pulmonary artery (*2*) in that back-flow is a significant feature of the curves presented here, whereas the curves of Baxter and Pearce, obtained in dogs with an implanted Pitot tube in the usual orientation, showed no back-flow.

In the pressure tracings from the distal point in the right pulmonary artery, the dicrotic notch and the postnotch rise in pressure are seen to occur later than in the tracings taken close to the valve. In fact, with some of the beats, the postnotch rise merges with the systolic rise of the next beat. That this rise is not due to atrial systole is shown by the lack of any constant temporal relationship between the rise in pressure and the appearance of the P-wave. Examination of the differential pressure curve shows that there is a significant forward flow associated with the post notch pressure rise, suggesting that this flow is due to a surge of blood rebounding from the valve and the arterial segment immediately distal to the valve following the retrograde flow noted above and the sudden closure of the valve. The systolic flow rises to a maximum (22 cm/sec) in two steps and returns quickly to minimal flow, the whole ejection lasting just over 0.3 sec. No sign of more than momentary and insignificant retrograde flow is noted at this point in the artery.

The method is not technically difficult. A properly modified double-lumen catheter is required in which the dynamic characteristics of the two lumina are identical. Pressure transducers of equal sensitivity connected to a recording apparatus that can produce a signal pro-

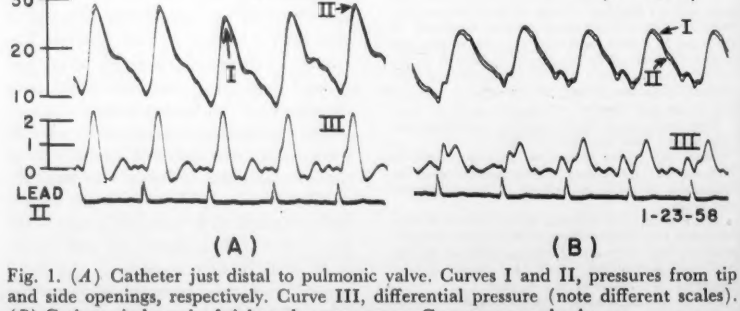

Fig. 1. (*A*) Catheter just distal to pulmonic valve. Curves I and II, pressures from tip and side openings, respectively. Curve III, differential pressure (note different scales). (*B*) Catheter in branch of right pulmonary artery. Curves same as in *A*.

portional to the difference between the signals from the transducers are also needed. The most troublesome problem has been the elimination of any factor tending to modify the dynamic characteristics of one lumen with respect to the other. Very fine bubbles in the system that do not visibly affect the pressure tracings can so change the characteristics of one lumen that the differential pressure tracing is seriously degraded.

It is believed that the method provides a means of measuring the instantaneous linear velocity in any vessel having a significant rate of flow. Volume flow per beat, such as the stroke volume in the pulmonary artery, can be calculated from the differential pressure curves if some estimate of the diameter of the pulmonary artery is available. A square-front velocity distribution is assumed in such calculations because of the pulsatile nature of the flow (*3*). Values obtained can be checked by standard Fick output studies.

The method appears to have applicability in normal and pathological situations, in steady and nonsteady states, in animals and in man.

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16 April 1958

O-methylation, the Principal Route of Metabolism of Epinephrine in Man

Abstract. Evidence is presented which indicates that the principal pathway of metabolism of epinephrine in man is O-methylation to metanephrine. The extent of the conversion to metanephrine, a physiologically inactive compound, indicates that the enzyme responsible for this reaction, catechol-O-methyl transferase, is the enzyme mainly involved in the termination of action of epinephrine in man.

For many years monoamine oxidase has been considered to be the primary enzyme in the metabolism of epinephrine. However, recent work in this laboratory has demonstrated that epinephrine and norepinephrine are transformed in the rat mainly by O-methylation to yield metanephrine (*m*-O-methyl-epinephrine) and normetanephrine (*m*-O-methyl-norepinephrine) (*1*). This reaction has been shown to be catalyzed by the enzyme, catechol-O-methyl transferase (*1, 2*). It was of interest, therefore, to determine the extent of O-methylation of epinephrine in man.

Table 1. Fate of β-H^3-epinephrine in man.

Subject	Radioactivity excreted in urine: As percent of administered dose	Percent of urinary radioactivity present as: Metanephrine: Free	Metanephrine: Conjugated	Metanephrine: Total*	VMA†
		β-H^3-epinephrine administered			
R.C.	95	13	46	59	30
D.K.	95	14	38	52	37
R.B.	88	11	36	47	35
D.H.	73	10	49	59	40
		β-H^3-metanephrine administered			
W.N.	92	16	39	55	24
K.S.	88	11	33	46	25

* Metanephrine found after heating in 1*N* HCl for 30 minutes at 100°C. Conjugated metanephrine represents the difference between free compound and total. A small amount of metanephrine glucosiduronic acid (6 percent) is included in the conjugated fraction.
† 3-Methoxy-4-hydroxymandelic acid (vanillylmandelic acid). This fraction also contains an unidentified metabolite which represents about 5 percent of the total radioactivity in the urine.

One milligram of *d,l*-β-H^3-epinephrine bitartrate (267 μc) was given intravenously over 45 minutes to four normal young male subjects, and the urine was collected for 48 hours. During this time, 73 to 95 percent of the administered radioactivity appeared in the urine (*3*). Metanephrine was extracted into isoamyl alcohol at *p*H 10, and the extract was assayed for radioactivity (*3*). On Whatman No. 1 paper the extracted radioactive material exhibited a single peak having the same R_F as authentic metanephrine (*1*) after chromatography in butanol–acetic acid–water (8:2:2) and isopropanol–5 percent ammonia (8:2). The 3-methoxy-4-hydroxymandelic acid was extracted at *p*H 1 into isoamyl alcohol. The extract was shaken with 5 percent sodium bicarbonate; the aqueous layer was re-extracted into isoamyl alcohol at *p*H 1, which was assayed for radioactivity (*3*). After chromatography, using the systems described above, the final extract showed a major peak having the same R_F as authentic 3-methoxy-4-hydroxymandelic acid and a small peak representing an unidentified compound present to the extent of 5 percent of the total radioactivity in the urine. All determinations of radioactivity were made by using internal standards and were corrected for the partitions of the O-methylated metabolites in the two-phase systems described above.

Free and conjugated metanephrine (Table 1) accounted for 54 percent of the radioactivity in the urine. These results differ from those published by others (*4*) in which little metanephrine was found in the urine following the infusion of C^{14}-epinephrine to man. We also found that 3-methoxy-4-hydroxymandelic acid accounted for 36 percent of the radioactivity in the urine (Table 1). Armstrong and McMillan (*5*) have reported the latter compound to be a major metabolite of norepinephrine.

To examine the relative importance of deamination in the metabolism of epinephrine, the metabolism of its major product, metanephrine, was studied.

About 0.7 mg of β-H^3-metanephrine (*6*) was administered intravenously to two normal young males over 45 minutes, and urine was collected for 48 hours. In contrast to the marked physiological and psychological effects produced by β-H^3-epinephrine, no detectable effects accompanied infusion of β-H^3-metanephrine. As in the case of β-H^3-epinephrine, 88 to 92 percent of the radioactivity was excreted in the urine. Essentially the same fraction of the administered radioactivity was excreted as metanephrine (free and conjugated) after administration of β-H^3-metanephrine as was found after administration of β-H^3-epinephrine (Table 1). A considerable proportion of administered metanephrine was deaminated and excreted as 3-methoxy-4-hydroxymandelic acid, indicating that a significant fraction of the metanephrine arising from epinephrine is further metabolized to 3-methoxy-4-hydroxymandelic acid.

These results indicate that the role of monoamine oxidase in epinephrine metabolism is mainly in the deamination of metanephrine. This would explain the observations that iproniazid, an inhibitor of monoamine oxidase, does not prolong the physiological actions of epinephrine in vivo (*7*).

From our results it can be concluded that the principal pathway of metabolism of epinephrine in man is its O-methylation to metanephrine, which in turn is conjugated and deaminated.

This, together with the lack of physiological and psychological action of 3-O-methyl catechol amines observed by others with normetanephrine (*8*) and by us with metanephrine, points to catechol-O-methyl transferase as the principal enzyme for the inactivation of epinephrine.

Note added in proof: Since this communication was submitted for publication, a paper by Kirshner *et al.* (*9*) has appeared which reports that 47 percent of the radioactivity in the urine is "3-methyl-O-adrenaline" (metanephrine), free and conjugated, following the administration of *d,l*-adrenaline-2-C^{14} to man. This finding differs from that reported previously by these workers (*4*).

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16 July 1958

Evidence That the Mammalian Nephron Functions as a Countercurrent Multiplier System

Abstract. Fluid collected by micropuncture from the bend of the loop of Henle in the concentrating hamster kidney had the same osmotic pressure as fluid from a collecting duct at the same level, while that from the distal convolution was more dilute. This indicates that the tubular fluid is first concentrated, then diluted, before its final concentration.

Hargitay and Kuhn (*1*), in 1951, introduced a new and revolutionary concept for the mechanism of urine concentration in the mammalian kidney based on the premise that the loop of Henle acts as a countercurrent multiplier system. The loop of Henle mechanism was thought to make the interstitium of the medulla hyperosmotic, which in turn caused diffusion of water out of the collecting ducts and concentration of the urine. The great theoretical advantage of this mechanism is that at no level in the kidney need there be large osmotic gradients maintained by tubular structures only one cell layer thick.

The original experimental observations in support of this theory were those of Wirz, Hargitay, and Kuhn (*2*), who concluded from cryoscopic studies of slices from concentrating rat kidneys that the osmotic pressure was identical for all adjacent tubular structures at any level in the kidney, and that there was a steadily increasing osmotic gradient from the cortex, which was isosmotic with plasma, to the tip of the papilla. Recent analyses of distal tubular fluid by Wirz (*3*) and ourselves (*4*) demonstrate that fluid in all adjacent tubules does not have the same osmolality, invalidating this aspect of the original data which presumably was due to postmortem diffusion. This does not, however, invalidate the theory of increasing osmotic gradient from cortex to papilla. This report (*5*) presents the results of osmolality determinations on fluid collected directly from the loops of Henle of hamsters.

The papilla of the hamster's kidney, which extends into the upper portion of the ureter, was exposed in anesthetized animals. When observed microscopically, vasa recta and collecting ducts were readily apparent. Under proper illumination, segments of narrow tubular structures filled with clear fluid were sometimes visible. When punctured with a micropipette and filled with large amounts of dye, they were seen to form typical hairpin loops without anastomosis. On occasion it was subsequently possible to macerate the kidney and to follow the injected loop by microdissection to the proximal and distal convolutions of a juxtamedullary nephron, proving beyond doubt that the structure punctured in the papilla was a loop of Henle. In order to exclude the possibility that the sample was plasma from a vas rectum without red cells or anastomosis, it was sufficient to demonstrate that the sample contained little or no protein by qualitatively testing it with heat or trichloroacetic acid. Fluid was also collected from adjacent collecting ducts at the same level. Osmolality was determined by the microcryoscopic method of Ramsay and Brown (*6*).

The results of four typical analyses of fluid from the bends of the loops and collecting ducts are shown in Table 1. The osmolalities were the same or nearly so and were much higher than the osmolality of plasma from the inferior vena cava. Fluid from cortical segments of proximal tubules and late distal convolutions was isosmotic and from early distal convolutions, hypo-osmotic to plasma.

Table 1. Osmolality of fluid from the loops of Henle and collecting ducts and of plasma from the inferior vena cava.

Hamster No.	Osmolality (milliosmoles per kilogram of water)		
	Loop of Henle	Collecting duct	Plasma
1	1391	1402	308
2	725	720	336
3	1270	1206	325
4	453	453	

These results are highly consistent with the hypothesis of Hargitay and Kuhn (*1*) that the mammalian nephron functions as a countercurrent multiplier system to concentrate the urine. The details of the mechanism appear to be somewhat different from those first proposed (*7*).

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12 June 1958

A System of Names for Binary Numbers

Abstract. A nomenclature is proposed for the binary number system to permit expression of binary numbers in words and to encourage visualization of magnitudes expressed in binary notation without recourse to decimal translation.

Our everyday lives impinge increasingly on systems in which binary numerical notation is encountered—for example, computers, data-processing systems, accounting systems, counting devices, logical circuitry, communication, and instrument systems generally. Familiarity with binary notation and some ability to think in terms of binary arithmetic are necessary for all scientists and engineers and are desirable for any well-informed

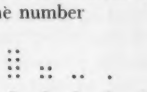
individual. It may well prove useful to arm every school child with skill in binary numbers.

The extreme simplicity of the binary system should make it a simple matter to achieve widespread acquaintance with its manipulation, provided that its use is not made to depend on a basic understanding of the mechanism of positional-notation number systems. More especially, its use should not depend implicitly or explicitly on conversion of binary numbers to or from decimal numbers. It is the purpose of this report to present a system of names that will permit expression of binary numbers without dependence on any other number system. To make this presentation self-sufficient for the benefit of those who have had no previous acquaintance with binary numbers, and to demonstrate the independent derivation of the binary number system, a brief description follows.

A binary number consists of a sequence of two alternative symbols, usually 0 and 1, as for example:

1 0 1 0 0 1 1 0 1 0

Each position in the sequence represents double the value of the position to its right and half the value of the position to its left. Assignment of unit value to a particular position fixes the values of all positions. The unity position is identified by placing a dot (.) called the binary point, to its right, thus: 10100.1010. If the point is omitted, the unity position is understood to be the ultimate position at the right end of the sequence. The value of a number is the sum of the position values specified by the symbol 1. The symbol 0 identifies the position values to be omitted from the sum. For example, the number

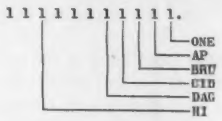


in which the value of each position is given by the number of dots in the array over the position, represents the number

The rules of binary arithmetic include only one that is unique to the binary system: $1 + 1 = 10$. Thus:

$$0 + 0 = 0$$
$$1 + 0 = 1$$
$$1 + 1 = 10$$
$$1 \times 1 = 1$$
$$1 \times 0 = 0$$
$$1 - 1 = 0$$

The inability of the reader to express in words the rule $1 + 1 = 10$ illustrates the lack of names for binary numbers. The names now proposed are as follows: The terms *one* (1) and *zero* (0) are retained for the symbols with the usual meanings of unity and nought. Position value names are

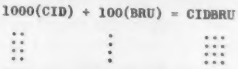


In assigning these names a mnemonic has been introduced that takes advantage of the widespread knowledge of Latin alphabetic order by making the initial letter of the name correspond to the binary order of magnitude.

If the proposed nomenclature is to serve its purpose, these names must become mentally associated not with decimal equivalents but directly with magnitudes, as shown in Table 1. Note that the use of the comma to set off groups of positions (in groups of bru) also serves to reduce confusion with the decimal system (in which groups of ap one are used).

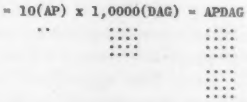
Numbers not specifically named are expressed as sums and products of the named values analogous to conventions used with the decimal system, thus:

1100 = 1000(CID) + 100(BRU) = CIDBRU



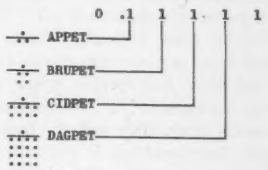
(the larger value "cid" being named first signifying *addition*) and,

10,0000 = 10(AP) x 1,0000(DAG) = APDAG



(the smaller value being named first signifying *multiplication*).

Fractional positions (to the right of the binary point) are to be named by adding the suffix *-pet* (a degradation of the word *part*) to the name of the reciprocal integral position, thus:



The number 0.11 is apone brupets

or the equivalent, bruap cidpets

It is interesting to compare the number of terms needed in the binary system and in the decimal system to express numbers up to the magnitudes included here. In the decimal-number nomenclature we have zero, one, two, three, four, five, six, seven, eight, nine, ten, hundred, and thousand—a total of thirteen terms. In the binary-number nomenclature we have zero, one, ap, bru, cid, dag, and hi —a total of bruapone (seven) of which bruone (five) are new.

Comparison of the number of syllables needed to express numbers in the two systems is unfavorable to the binary system, and long sequences become awkward at values much smaller than they do in the decimal system. It is not necessary, however, to go beyond the magnitudes named here (*1*) to achieve the primary purpose of this proposal, which is development of the ability to "think binary." Long sequences can be communicated by calling off the sequence of digits, just as is done, for example, in relaying telephone numbers.

A few additional examples of number names are shown in Table 2. Finally, the arithmetic rule $1 + 1 = 10$, which we could not previously express, is now: One and one are ap.

Table 1. Names, symbols, and magnitudes of binary numbers.

NAME	SYMBOL	MAGNITUDE
ZERO	0	
ONE	1	·
AP	10	··
BRU	100	∴
CID	1000	∴·
DAG	10000	∴··
HI	1,0000,0000	∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴

Table 2. Examples of number names.

Decimal	Binary
297	1,0010,1001
Two hundred ninety-seven	Hiapdagcidone
87	101.0111
Eighty-seven	Bruonedag bruapone
58.375	11,1010.011
Fifty-eight and three hundred seventy-five thousandths	Aponedagcidap and apone cidpets

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Note

1. It has been suggested by G. W. Patterson of the Moore School of Electrical Engineering that the usefulness of the proposed system of names would be very much enhanced if the system were extended by adding means for expressing powers of hi. He suggests bihi, and so forth, for this purpose. While the author is largely in agreement with this point of view he has preferred to allow extension of the system to await demonstrated need. Appreciation is due Professor Patterson for critical review of the proposal and for a number of useful suggestions.

25 June 1958

Some Genetical Implications of Physical Studies of Human Haptoglobins

Genetical differences obtained with human and cattle serum proteins have been demonstrated by the technique of starch gel electrophoresis (*1*, *2*). These proteins in man, which are known as haptoglobins, migrate with the α_2-globulins and have the specific property of binding hemoglobin (*1*). Family studies are usually compatible with the hypothesis that their synthesis is controlled by two autosomal genes with incomplete dominance (*3*). It has been proposed that the three genotypes should be designated Hp^1/Hp^1, Hp^2/Hp^1, and Hp^2/Hp^2 (*4*).

The electrophoretic differences which first enabled classification of human sera into the three groups are complex and are shown diagrammatically in Fig. 1, column 2. The serum corresponding to group 1–1 contains a protein with a mobility in the fast α_2 fraction which, when combined with hemoglobin, stains with benzidine, whereas that designated group 2–2 has three bands of slower mobility which also stain with benzidine when combined with hemoglobin. Although the heterozygote, group 2–1, also shows a weak band corresponding in position to the fast α_2-globulins, the three slower bands differ from those in the group 2–2 serum in position and relative intensity. An even greater degree of complexity is suggested by the frequent presence of additional hemoglobin binding proteins in trace amounts.

Electrophoretic separation of hemolyzed serum by conventional starch zone electrophoresis also enables a distinct differentiation of the three groups to be made. When this method is used, the red band of the haptoglobin-hemoglobin complex can be seen against the white starch background. The diagrams in Fig. 1, column 3, show that the most rapidly migrating red band is found in group 1–1, whereas the slowest corresponds to group 2–2. The heterozygote does not separate into two discrete colored zones, as might have been anticipated, but migrates as a single band of intermediate mobility. These observations are in striking contrast to many of the hemoglobinopathies in which the heterozygote usually reveals a mixture of the two components found in the homozygotes.

To investigate these proteins further, samples of the haptoglobin-hemoglobin complex of the three genetic groups were purified in the following manner. Fifteen to twenty milliliters of serum free from hemolysis were separated by starch-zone electrophoresis (barbital buffer, *p*H 8.6, $\Gamma/2$, 0.1). The α_2-globulin peak was eluted and concentrated, and hemoglobin C was added in sufficient quantity to ensure saturation of the hemoglobin-binding capacity of the haptoglobin. The mixture of α_2-globulin and hemoglobin C was separated on a second starch block (barbital buffer, *p*H 8.6, $\Gamma/2$, 0.05). The presence of hemoglobin C resulted in sufficient slowing of the haptoglobin-hemoglobin complex to allow it to be seen as a red band behind the other α_2-proteins and ahead of the excess free hemoglobin C. Hemoglobin A, which migrates more rapidly, causes less slowing of the haptoglobin complex and therefore results in poorer separation of the haptoglobins from the remainder of the α_2-globulins. Purified preparations of haptoglobin-hemoglobin complex from each of the three hemoglobin types were then studied in the ultracentrifuge (Fig. 1, column 4).

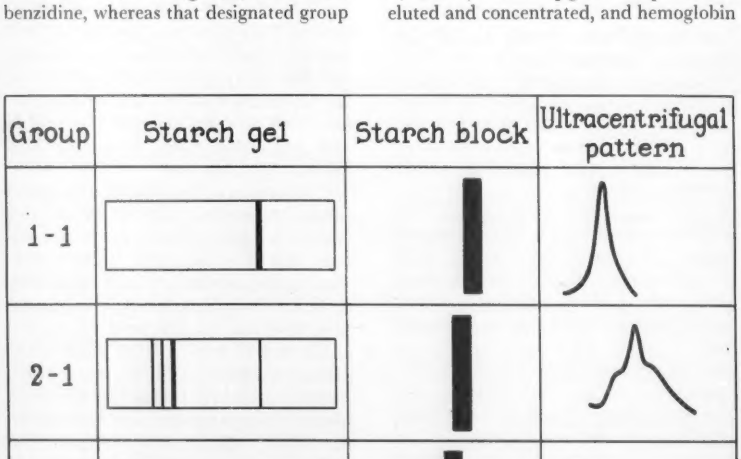

Fig. 1. Comparison of the starch gel, starch block, and ultracentrifugal patterns of the haptoglobin-hemoglobin complexes from the three main genetic groups.

Each of five specimens isolated from the sera of two individuals of group 1–1 had a single protein peak with an approximate sedimentation (s) rate of 6 *S* (5.4 to 6.3), whereas the predominant peak in six samples from three homozygotes corresponding to group 2–2 sedimented with an s rate of approximately 10 *S* (9.4 to 10.7). Because of dependence on concentration, these would correspond to $s^0_{20,\,w}$ values of approximately 6 and 11 *S* and are similar to the values reported by Jayle *et al.* (*5*) for two types of haptoglobin-hemoglobin complexes. In the heterozygote, however, each of eight fractions isolated from three individuals contained a major component with an s rate of about 8 *S* (7.6 to 8.8) and an approximate $s^0_{20,\,w}$ of 9 *S*. In addition, there were two minor components with s rates essentially similar to those present in the homozygotes. No material with an s rate of 8 *S* was detectable in either homozygote. Electrophoretically isolated α_2-globulins from two individuals of groups 1–1 and 2–2 were mixed in varying proportions, and hemoglobin C was added to saturate the haptoglobins present. The haptoglobin-hemoglobin complex of this "synthetic heterozygote" was then isolated and studied in the ultracentrifuge. Two distinct peaks with s rates of approximately 6 and 10 *S* were observed. No peak of intermediate sedimentation rate, such as was seen in the "true heterozygote," could be seen.

The presence of three different haptoglobin groups was also reflected by the distinct differences in the ultracentrifugal behavior of the whole α_2-globulin fractions, with and without added hemoglobin (*6*).

It is apparent that the two genes at the haptoglobin locus have given rise to three, and possibly more, closely related proteins some of which can be distinguished ultracentrifugally. One of these appears to be confined to the heterozygote. These findings in man bear some

similarity to the hybrid substance described by Irwin which occurs in doves (*7*), and, more particularly, to the extensive observations of Cohen on some of the red cell antigens in the rabbit in which genetic interaction has been amply demonstrated (*8*). These results may also be relevant to the problem of heterotic vigor and illustrate how this phenomenon might on occasion be due to the presence, in the heterozygote, of a substance not possessed by either homozygote (*9, 10*).

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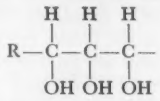
31 March 1958

Isotope Effect in Oxidation of D-Mannitol-2-C^{14} by Acetobacter suboxydans

Previous reports from this laboratory have described the preparation of D-mannitol-1-C^{14}, its oxidation by *Acetabacter suboxydans*, and the carbon-14 assay of the resulting D-fructose-1,6-C^{14} (*1–3*). Because the two halves of the mannitol molecule are stereomerically identical, oxidation by *A. suboxydans* can take place at either carbon 2 or carbon 5. It was pointed out that "if oxidation took place without either an isotope effect or breakdown of the D-mannitol and resynthesis of the fragments, the derived D-fructose would be labeled equally and exclusively at carbons 1 and 6" (*3*). The early work showed that, within the error of measurement, D-fructose-1,6-C^{14} was, indeed, labeled equally and exclusively at carbons 1 and 6.

Oxidation of glycitols by *A. suboxydans* is specific for the group



where R is either H or certain other substituents. Presumably, the enzyme responsible for the oxidation forms an intermediate complex that involves the three carbon atoms indicated. The presence or absence of an isotope effect in the oxidation of a labeled D-mannitol should provide information concerning the rate-determining step, and hence, the mechanism of reaction.

In a more extensive study of a possible isotope effect, both 1-C^{14}- and 2-C^{14}-D-mannitol have been oxidized by *A. suboxydans*. The distribution of carbon-14 in the resulting D-fructose-1,6-C^{14} and D-fructose-2,5-C^{14} has been determined by several chemical methods, selected to avoid isotope effects in the analysis.

The results, summarized in Table 1, confirm the earlier radioactivity analysis of D-fructose-1,6-C^{14}; no isotope effect was detected. However, a small disproportionation in the distribution of carbon-14 was found for D-fructose-2,5-C^{14}. This indicates that, in the oxidation of D-mannitol-2-C^{14} by *A. suboxydans*, there is a small isotope effect, and oxidation is slightly less rapid at carbon 2 (C^{14}) than at carbon 5 (C^{12}).

Because of the extensive use of C^{14}-labeled products in biochemical studies, the demonstration of an isotope effect in a biological oxidation is particularly significant. Although the effect is small, it shows the need for caution in the use of biological oxidations for determining the distribution of carbon-14 in carbohydrates.

All of the compounds listed in Table 1 were recrystallized to constant radioactivity, and samples were assayed in solution (*4*).

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Table 1. Radioactivity analysis of D-fructose-1,6-C^{14} and D-fructose-2,5-C^{14}.

Compound assayed	Carbon atoms of original D-fructose	Radioactivity after successive recrystallizations (μc/mmole)	Av. % of original radioactivity
Analysis of D-fructose-1,6-C^{14}			
D-Fructose-1,6-C^{14}	1, 2, 3, 4, 5, 6	2.62*	100
Potassium D-arabonate	2, 3, 4, 5, 6	1.32*	50.4
"D-Glucose" phenylosotriazole†	1, 2, 3, 4, 5, 6	4.35, 4.33, 4.34	100
4-Formyl-2-phenylosotriazole‡	1, 2, 3	2.15, 2.17, 2.16	49.8
Dimedon-formaldehyde compound§	6	2.17, 2.18	50.1
Analysis of D-fructose-2,5-C^{14}			
D-Fructose 2,5-C^{14}	1, 2, 3, 4, 5, 6	1.93, 1.96, 1.93	100
"D-Glucose" phenylosotriazole†	1, 2, 3, 4, 5, 6	1.94, 1.90, 1.91	
4-Formyl-2-phenylosotriazole‡	1, 2, 3	0.93, 0.94, 0.93	48.4
Erythritol	3, 4, 5, 6	0.97, 0.98, 0.99	51.4
Erythritol tetrabenzoate	3, 4, 5, 6	1.01, 1.00, 0.99	
Dimedon-formaldehyde compound§	6	none	

* Value taken from Frush and Isbell (*3*). † D-*arabino-Hexose* phenylosotriazole. ‡ Phenyl-2*H*-1,2,3-triazole-4-carboxaldehyde. § 2,2′-Methylenebis(5,5-dimethyl-1,3-cyclohexanedione).

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7 April 1958

Iodine-131 Fallout in Bovine Fetus

Iodine-131 from radioactive fallout is concentrated in thyroid glands of grazing animals (*1, 2*) and the distribution suggests that I^{131} spreads over the hemisphere in which it is released (*2*). A study of the fallout of I^{131} in the thyroids of fetal animals will serve two purposes: (i) It will be helpful in evaluating the maximum biological accumulation of radioactive fallout; and (ii) it might give useful information regarding iodine distribution during pregnancy.

Gorbman *et al.* (*3*) injected I^{131} into two cows during the ninth month of pregnancy, sacrificed them 24 hours later, and studied the I^{131} distribution. They found that the I^{131} concentrations in the thyroid of the fetuses were 6 to 7 times those of the dams. Autoradiographs showed uniform distribution of radioactivity in fetal glands but nonuniform concentrations in the adult thyroids. Wolff *et al.* (*4*) showed that bovine fetuses began to concentrate iodine at 53 days of gestation and that the amount of iodine increased rapidly after the fifth month.

Barnes *et al.* (*5*) have studied I^{131} distribution in pregnant sheep which were chronically fed the radioisotope. They showed that the near-term fetal thyroid I^{131} concentration was 1 to 2 times that of the dam.

Part of one lobe of the thyroid gland from each of 40 pregnant cows was removed along with the laryngothyroid

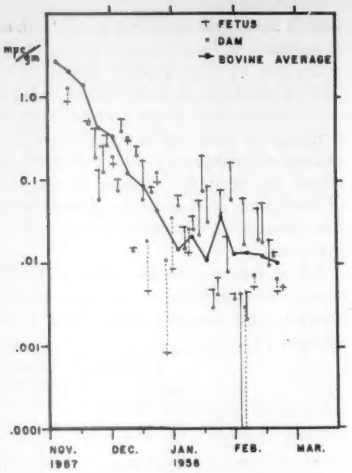

Fig. 1. Semilogarithmic average course of I^{131} fallout concentrations in thyroids of 400 arbitrarily selected cattle (solid circles). The open circles and crosses represent thyroid I^{131} concentrations of pregnant cows and of their fetuses. The solid vertical lines connecting circles and crosses represent cases in which I^{131} of the fetus exceeded that of the dam. A broken line is used when I^{131} of the dam exceeded that of the fetus.

areas of their fetuses. Whole thyroid weights were used as the best index of fetal age because this was the only accurate index of fetal size that could be made in our laboratory. Accurate histories of the animals were not available, but it is thought that most of the adult animals had grazed within 200 miles of Memphis, Tenn., and that they were kept in feed lots less than 1 week.

Iodine-^{131} was determined as described previously (*2*). Two fetal-dam combinations are not included in the graphs because the amounts of I^{131} were too small to measure accurately.

Figure 1 compares the I^{131} in thyroids of bovine fetuses and their dams with the curve showing concentrations in thyroids of other cattle from the same general area. The curve of average I^{131} content was determined from 400 thyroids by measuring the concentration of thyroid I^{131} in 7 to 10 unselected cattle slaughtered every Monday, Wednesday, and Friday. The average values for each week were plotted. The individual maxima and minima for each week differed by one logarithm scale during the period November to 15 December, after which the range increased to 1.4 log scales. The increased range was primarily due to relatively higher maxima after 1 January. The slope of the average curve from November to January suggests an average effective half-life of approximately 8 days for the two months following the nuclear tests conducted in the fall of 1957. After 1 January the change in slope of the average curve was probably due to new fallout. The fetal thyroid I^{131} concentrations all lie within the maximum range of normal adult animals.

Figure 2 shows the F/D ratio—that is, (fetal I^{131}/g of thyroid)/(dam I^{131}/g of thyroid)—versus the fetal thyroid weight [intra-uterine ages were determined according to the method of Nichols *et al.* (*6*)]. Eighty-five percent of the 7- to 9-month fetuses had greater I^{131} concentration in their thyroids than did their dams. Only 68 percent of the 6- to 7-month fetuses had more I^{131} in their thyroids than did their dams. These data suggest a progressive increase in F/D ratio as the fetuses matured; however, the points are probably not a two-variable normal distribution. The maximum F/D ratio found in these animals is not as great as that found 24 hours after I^{131} injection into pregnant cattle (*3*). This difference in F/D ratio may be related to differences in I^{131} exposure or to metabolic differences between the cattle used in the injection experiments and the animals reported here.

If any relation exists between the thyroid concentration of I^{131} and intra-uterine age as a function of the age of the fallout, it is not revealed by these data.

Chemical iodine has not been determined in the glands reported here, but the data of Wolff *et al.* (*4*) may be comparable. From their data it can be calculated that between 6 and 7 months of gestation, the bovine fetal thyroid had approximately one-half the concentration of I^{127} (0.55 to 0.7 mg/g of gland) as the normal cow (1.5 mg/g). Figure 2 suggests that at this same intra-uterine age (6 to 7 months) the average fetal thyroid had a slightly greater I^{131} concentration than the gland of the fetus' dam. The values for I^{127} concentration in newborn calves overlapped with the range for normal cows (*4*), but near term (7 to 9 months) I^{131} concentration in the fetal thyroid approached twice that in the dam's thyroid.

One interpretation of such results is that approximately one-half of the thyroid iodine in the dams had turned over in 6 weeks, but it may have turned over more than once. This follows if we consider the near-term fetal thyroid specific activity to approach a maximal value and if the specific activity of the adult glands remained approximately one-half that of the fetuses while there was no new I^{131} increment. This would suggest that some of the thyroid iodine pools may turn over rapidly and other pools may turn over much more slowly. This might mean that a large fraction of the thyroid iodine in the dam may be almost static. Similar differences in thyroid iodine pools were suggested by Stanbury *et al.* (*7*) and by autoradiographic studies by Gorbman *et al.* (*3*). Those cases near term in which the F/D ratio is less than 1 may illustrate dams removed from fallout, and in some cases the fractional rate of turnover of large slow pools may more nearly approximate that of the fast pools (*8*).

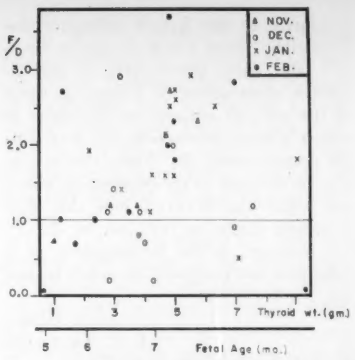

Fig. 2. (Thyroid I^{131} concentration of fetus)/(thyroid I^{131} concentration of dam) versus weight of fetal thyroid. These data represent the same animals illustrated individually in Fig. 1. The four types of points (triangles, open circles, crosses, and solid circles) show the month in which the animals were slaughtered, and this helps to locate the pairs on Fig. 1. The approximate fetal ages were derived from the thyroid weights (*3*). Thyroids of newborn calves were reported to average 5 g (*4*).

Note added in proof. Forty-two additional fetal-dam pairs were studied over the succeeding 4 months. Fourteen of these were in the fourth or fifth month of gestation with F/D ratios less than 1 in 12 of the fourteen pairs; 20 specimens were approximately at the 6-month stage, with an average ratio of 1.7 (± 1.0). Eight were in the last 3 months of gestation, with F/D ratios averaging 2.7 (± 2.2); one of these had a ratio less than 1, and one a ratio of 7.

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24 March 1958

Meetings and Societies

Chemical Basis of Development

The McCollum Pratt Symposium on the Chemical Basis of Development was held 24–27 March 1958 at Johns Hopkins University. The program was opened by B. H. Willier, who traced the development of embryology in the United States, from the work of Louis Agassiz through that of the Johns Hopkins and Chicago schools.

Clement L. Markert said that the major problem of embryology is the study of development as a dynamic process and cited experiments indicating that the chemical environments condition the further development of the cell. He pointed out that embryonic cells produce qualitatively different products in mixed culture and in pure culture and that this suggests an interaction among cells that results in new enzymes. He proposed the possibility that the genes are not the same in cells from embryo to adult form and suggested that the manifestation of gene activity is perhaps only possible at certain levels of differentiation. He cited experiments on the esterases of mouse tissue, of which there are approximately 20, separable by electrophoretic mobility. Varying patterns developed during successive stages of differentiation of mouse liver. Furthermore, liver cells in tissue culture lose most of their esterases, even though they continue to grow. The hypothesis was proposed that the chromosomes of the fertilized egg are not identical with the chromosomes of the adult and may acquire new proteins, thus altering their activity. These proteins might possibly be the inducers.

R. D. Allen described a study of the cortical granules and their role in the development of the fertilization membrane of the *Arbacia* egg. Since the latent period of the cortical reaction is temperature-dependent, the reaction is probably chemical. Experiments with eggs in capillary tubes indicate that the fertilization membrane is the result of local reactions. Heat or pressure can prevent the extension of the fertilization membrane. Thus, an egg elongated in a narrow capillary could be fertilized at both ends. Allen measured the rate of conduction of the cortical reaction in the egg and found that the Q_{10} is dependent upon the stretching of the membrane. These experiments give further support to Loeb's hypothesis of surface cytolysis as the mechanism of the development of the fertilization membrane. Indeed, the surface cytolysis proposed by Loeb may actually be a lytic process around the cortical granules.

F. E. Lehmann of the University of Bern discussed the pole plasm, which is Nadi reactive. It accumulates around the vegetive and animal poles and can be centrifuged to either pole without altering development. However, experiments with displacement by centrifugation of the pole plasm to regions other than the vegetive poles produced eggs which did not divide. Experiments with the displacements of the spindle demonstrate also that intracellular organization of the blastomere is as important as the intercellular organization of the blastema in embryogenesis.

A. E. Mirsky's experiments on nuclear differentiation and function were based on three postulates: (i) that there are the same chromosomes in the nucleus of the salivary gland of *Drosophila* as in the sperm and egg; (ii) that there is constancy of deoxyribonucleic acid (DNA) content of the nucleus; and (iii) that the histones of all cells are similar. He showed that there is a high-energy generating system in the nucleus which produces adenosine triphosphate (ATP) separately from the cytoplasmic system. Deoxyribonucleic acid is apparently a cofactor in ATP synthesis. The meaning of the expression *cofactor* was discussed, and the conclusion was drawn that DNA is "necessary" for the formation of ATP, but there is no direct evidence for a catalytic role of DNA in this formation of ATP in the nucleus. The amount of nucleotide in the nucleus is related to the amount of ATP in the nucleus. Evidence was also presented for the influence of the adjacent cytoplasm on nuclear activity and for a biochemical response to cytoplasmic changes. For example, the nuclei of the pancreas of a fasting animal are much less active than the nuclei of the pancreas of a fed animal. Two reports were cited as indicating that the nucleus operates in a sodium environment. Although there is some potassium in the nucleus, the sodium content is apparently much higher than the potassium content. If potassium is kept constant in the medium, sodium ion stimulates nuclear protein synthesis as measured by the uptake of labeled glycine. The sodium concentration that has the highest effect is approximately 0.065*M*. Abelson's experiments with the frog oocyte, in which it was shown that the nucleus concentrates Na^{24}, were also cited. Evidence for the differentiation of the nucleus was cited, such as the presence of hemoglobin within the nucleus of red cells, the fact that there is no myoglobin in the nuclei of muscles, and the variation in the ratio of nuclear to cytoplasmic arginase in different organs, such as liver and kidney. Furthermore, the nucleus is impermeable by certain antibodies which do permeate the cytoplasm. Stone's demonstration of the dedifferentiation of iris to lens must indeed involve a nuclear change. As special effects of the nucleus on the cytoplasm, the following were cited: first, that deoxyribonucleic acid synthesis, as demonstrated by Hogeboom and Schneider, is a function mainly, if not exclusively, of the nucleus; second, that the nucleus dominates ribonucleic acid synthesis, which controls protein synthesis in the cytoplasm. Finally, that nuclear deoxyribonucleic acid controls synthesis of ribonucleic acid in the nucleolus, which is much more active than the cytoplasm, as measured by the uptake of radioactive phosphate into ribonucleic acid of the nucleolus and the cytoplasm. A very interesting experiment which was cited by Mirsky involved the inhibition of synthesis of ribonucleic acid after treatment of the nucleus with deoxyribonuclease. This loss of ribonucleic acid synthesis could be restored by the addition of a number of different preparations of deoxyribonucleic acid.

J. Gall described the unusual structure of the lampbrush chromosome. Electron micrographs showed that there is a core strand in these chromosomes which is deoxyribonucleic acid, and that coiled around it is the mass of ribonucleic acid. At each node in the long lampbrush chromosome, lateral loops appear. These loops, too, are made of a central core of deoxyribonucleic acid, around which is apparently stretched ribonucleic acid. The action of deoxyribonuclease results in the formation of clumps of ribonucleic acid where the lateral loops had been. Experiments with stretching the lampbrush chromosome gave evidence for the loop nature of the lateral structures of the chromosomes.

Vincent cited some experiments concerning the nucleolar chemistry of the starfish. Apparently there are at least two forms of ribonucleic acid, based on the rate of uptake of P_{32}. There appear also to be two proteins in the nucleolus,

one of which has a histidine end group. Each of these proteins is associated with one of the ribonucleic acid fractions. The P_{32} is first taken up into ribonucleic acid of the nucleolus and then appears in the nucleotides.

M. V. Edds discussed the origin and structure of the intercellular matrix. Although the ground substance of cells is generally homogeneous, the mucopolysaccharide, even from adjacent areas, appears to be different. For example, the cornea contains mainly keratosulfate as the ground substance, with a small amount of chondroitinsulfate. On the other hand, the sclera contains mainly chondroitinsulfate and a small amount of keratosulfate. The function of mucopolysaccharide may be manifested through mucoproteins. The ground substance of cartilage appears to be chondroitinsulfate A and a noncollagenous protein. There is no obvious or immediate relation between the large molecules of the ground substance and the growth and development of the organism. Data on the crystallization of hydroxyapatites from metastable solutions of calcium or phosphate were given. Only normal collagen preparations will stimulate crystallization of the hydroxyapatites. Abnormal spacings of collagen result in no crystallization. The hypothesis is presented that mucopolysaccharides present in the tissues may prevent calcification of all collagens except that collagen which has the proper spacing. As an experimental model, unreconstituted collagen was demonstrated not to form apatites, whereas the normally reconstituted collagen will form apatites from metastable calcium and phosphate solutions.

Hewson Swift discussed the origin and function of cytoplasmic particulates, most of which, with the exception of the mitochondria, appear to be membranes. He described the various portions of the endoplasmic reticulum, including the cell membrane—for example, the infoldings of the kidney cell on electron microscopy. The other membranes are the nuclear membrane, the Golgi apparatus, the rough reticulum with its ribonucleic acid content, and the smooth reticulum. The ergastoplasm was described as sheets of membrane, highly basophilic, containing large amounts of ribonucleic acid, possibly involved in secretory function. In addition to these membranes there is a great deal of basophilic material apparently not associated with membrane. The studies of ribonucleic acid turnover with C_{14} adenine in *Drosophila* reveal several things: first, that ribonucleic acid is an integral part of the chromosomal material—a finding which is consistent with Gall's studies on the lampbrush chromosomes. Further, the ribonucleic acid turnover, as evidenced by the uptake of C_{14} adenine, showed that the chromosomal ribonucleic acid is most active, the nuclear next active, and the cytoplasmic least active. There does not seem to be a particulate component containing ribonucleic acid which is common both to nucleus and to cytoplasm. There are filaments projecting through both sides of the nuclear membrane, and these filaments appear to be ribonucleic-acid–containing.

T. Yamada discussed embryonic induction. Guinea-pig bone-marrow extracts, partially fractionated by centrifugation and ethanol precipitation, induced mesodermal and ectodermal development. Heat treatment of bone-marrow extracts produces a peculiar effect. Mesodermal activity is slowly destroyed with prolonged heating, but neural changes such as anencephaly, deuteroencephaly, and spinal cord effects appear after heat treatment and disappear with longer heat treatment. This differentiation between effects of the same bone-marrow extract suggests a multiple set of compounds capable of inducing particular tissue types. It was pointed out in the discussion that when a tissue type is induced by the bone-marrow extracts, it is an organized tissue type; this indicates that there must be intercellular reaction among the cells of a particular type to produce an organ-like structure, and that the inducer possibly might induce merely the "tendency" toward development of a certain type of tissue and not the organization of the tissue. This would be conditioned by the growth of the cells within that area.

M. Sussman reported on cellular interaction in slime mold development. There are two types of cells in each strain of slime mold. In a study of aggregation of slime molds it was found that the number of aggregation centers is proportional to the density of cells and that at optimal density the number of centers is proportional to the number of cells. He showed that there was a certain cell type directly related to the centers of aggregation, and he called this the "I" cell. This cell is anatomically different from the others in that it is several times larger. Centers can be caused to form (induced) by the insertion of an "I" cell into a colony of cells, and to achieve this effect the presence of the "I" cell is required for only about five minutes. The "I" cells are always present in a constant ratio to the total number of cells. This ratio is characteristic for the strain of mold. Evidence was produced that the "I" cells secrete or emit a diffusable substance. Mutant cells which do not aggregate can be caused to do so by the presence of A-type cells; this suggests an interaction of the A-type cells with "I" cells. A study, by Barbara Wright, of the substance (crazin) secreted by the "I" cells showed that urine of pregnant women and estrogenic substances had similar effects to crazin but that crazin itself had no estrogenic effect. Enzyme studies of the various growth stages of the slime mold show patterns characteristic of the general morphology and metabolism of the cell. For example, the amoeba form is an anaerobic form. The content of oxidative enzymes in these tissues is very low. The transition from amoeba to plasmodium is aerobic, and the enzymes of aerobic metabolism increase sharply at this point, particularly the Krebs cycle enzymes.

R. DeHaan discussed morphogenetic movements. Studies with acetylcholine as it affected the chick embryo led to the finding that the folding of the neural crest was inhibited by chelating agents. The effect was reversed by the addition of high concentrations of calcium to the medium. This led to the hypothesis that folding of layers is caused by a change in the surface of the cell, resulting in the appearance of calcium binding sites between adjacent cells. The calcium is then formed into a bridge which pulls the adjacent cells together, causing foldings.

Jean Pasteels described work on the comparative cytochemistry of cells, presenting experimental evidence for the specificity of cytochemical reactions of centrifuged eggs. He showed that, on centrifugation in various positions, similar types of stratification occurred in the three species examined. The various types of staining material went to the same pole in each species examined and formed bands of the same kind.

S. C. Shen discussed changes in enzymatic patterns during development. He used a copper thiol compound of choline as a substrate for the histochemically demonstrable choline esterase. In the formation of retina the first demonstrable choline esterase activity was on the surface of ganglion cells. After the bipolar neuron bodies appear, a choline esterase active layer develops between the synapses of the ganglion cells and the bipolar cells. Later this synapse layer splits into two, and finally four, layers of synapses, each set of synapses staining strongly for the choline esterase reaction. Further studies with the neuromuscular junction indicate a high choline esterase concentration right at the junction. Studies with amphibian muscle revealed that each muscle fiber received a nerve fiber only at the end of the cell, and that here alone is there choline esterase. However, the nerveless animal develops choline esterase in the tips of the muscle fibers at the same time as the control. If there is no innervation, due to the removal of the neural crest of that region, the choline esterase activity at the ends of the muscle disappears. As further demon-

stration that it is muscle cells which develop the choline esterase and that the initial stimulus need not come from nerve cell, muscle cells grown in tissue culture develop choline esterase. Both these sets of experiments suggested, in general, that choline esterase forms on the postsynaptic membrane without need for the presynaptic member for induction of the choline esterase activity.

Melvin Cohn reported on the induction and control of protein synthesis in development. In a study of permease it was found that a small molecule such as galactose can induce a change in the enzymatic composition of the cell that can be transmitted. It was further shown that, even if a few molecules of galactose remained in the progeny of the cell, the inducible enzyme will be present throughout the progeny. Therefore, induction is similar to mutation, for the progeny of the induced organism can maintain the enzyme as long as even a trace of inducer is present. If the inducer is completely removed, the cell reverts to the original type and the progeny can no longer be induced to form enzyme.

Werner K. Maas discussed the feedback inhibition of enzyme synthesis by-product as a controlled mechanism in enzyme synthesis. Using the enzyme ornithinetranscarbamylase, he found that formation of the enzyme is inhibited in *Escherichia coli* by arginine. This inhibition of ornithinetranscarbamylase synthesis can be demonstrated within a few minutes after the arginine content of the medium is increased.

Studies of the developmental aspects of nitrogen metabolism in amphibians were reported by Brown and Cohen, who showed that tadpoles excrete mainly ammonium ion as the nitrogenous waste, whereas frogs excrete mainly urea. The activity of the urea cycle enzymes in the liver is parallel to the ratio of urea to ammonia.

R. E. Eakin showed that the Needham data on the chick embryo excretion of nitrogen, which are still used as a demonstration of the rule that ontogeny parallels phylogeny, are incorrect. In the chick embryo there are not three cycles of nitrogen excretion, including intially an ammonia cycle, a urea cycle, and finally a uric acid excretion, similar to that in the adult animal. It appears that the urea formed is derived almost exclusively from the arginine of the yolk, and that there is no urea synthesis cycle at any time in the development of the chick. The arginase concentration diminishes during the growth of the chick as the arginine is used up (converted to urea). Decrease in the amount of ammonia in the allantois is shown to be a dilution effect and not the result of excretion of ammonia by the embryo at any time. It is demonstrated that the formation of uric acid begins and increases to the adult level during the development of the embryo.

James Ebert discussed the formation of antibodies during development and pointed out that there is no convincing evidence of antibody formation by the embryo and, furthermore, that, following birth, there is a characteristic period of delay, variable among species, during which there is no antibody formation. The effect of organ grafts on homologous organs of the host was demonstrated by the grafting of adult spleen into nine-day chick embryo allantoic membrane. This causes a marked growth in the embryo. This is organ specific, occurring only in the thymus and liver and spleen. It is animal and species specific and is age specific in the chick, for the developing chick becomes resistant to this effect at approximately 18 days. There is a peak in the susceptibility to the graft shortly after hatching. This effect can be found in a microsomal and supernatant fraction but not in the nuclear or mitochondrial fraction of the homogenized graft. If the graft is in contact with the host long enough, the host is decomposed. This is called the graft against host reaction. Since all of the tissues which showed this reaction are reticuloendothelial tissues, it appears that whenever living cells capable of an immune reaction are put in contact with an individual incapable of forming antibodies, the graft reacts against the host with an immune reaction which destroys the host. This suggests an explanation of the well-known phenomenon in which the injection of bone marrow is followed by a slow reaction of the foreign material against the host. These delayed deleterious effects have only recently been studied and were described as sequelae of experiments in the prevention of radiation sickness by injection of bone marrow. The same type of serious reaction occurs in individuals with deficiency in antibody formation who are treated with bone marrow.

R. E. Billingham took issue with the statement that the embryo was incapable of an immune reaction, because, he said, there is a peculiar reaction developed in the embryo which is not manifested by antibodies but which changes the reactivity of the embryo to antigen. This he called the "tolerance response phenomenon." This phenomenon is seen in the red-cell chimeras, in which two different types of red cells can be found because of intermingling of the blood stream of nonidentical twins *in utero*. Once these chimeras are developed, they can receive, without reaction, transfusion of blood from one another. Experimentally, baby mice inoculated with spleen cells from a foreign strain are able to take skin grafts from this strain without rejecting the graft. They have, therefore, become tolerant to the foreign strain even though uninoculated litter mates reject the grafts. The foreign cells are apparently kept in the spleen, lymph nodes, white cells, and bone marrow, and not in the liver. This tolerance is not tissue specific, but it is absolutely genetically specific. Dizygotic cattle twins become chimeras through mixing circulation and will accept grafts from each other but not from brothers, sisters, or mother. Tolerance is not inversely proportional to time of injection. There appears to be an optimum time for response. This temporal variation is different for different strains in relation to the same host. On the other hand, the further apart the donor and recipient are in genetic constitution, the earlier must be the application of the sensitizing material. This phenomenon is an explanation of the reason why animals do not react to their own tissues. They apparently develop a tolerance response because the tissues are present at all times during the course of the development. If a tissue is segregated so that its protein can only with difficulty come in contact with its reticuloendothelial system, there is a possibility that the animal can be immunized against its own tissue. For example, guinea pigs can be immunized against their own sperm. This is probably because the sperm appear late in the course of the development of the animal and some of the sperm proteins are not present during the early development of the lymphoid system. Furthermore, it is possible to develop antibodies to the lens of the eye. The lens develops with no lymphoid drainage and with, apparently, "physiologic quarantine." Patients with Hashimoto's disease (an inflammatory disease of the thyroid gland) have been found to show antibodies to thyroglobulin. It seems that thyroglobulin escapes into the lymphatic system and there stimulates the formation of antibodies. These antibodies then attack the thyroid gland. Normally the thyroglobulin does not escape into the circulation. The brain has no lymphatic drainage, and brain tissue from an animal injected into the same animal can produce an immunologic response. Furthermore, the brain will accept a homograft. Therefore, it is not capable of immunologic response. If lymphoid tissue is injected into a one-day-old mouse, a runt is produced which is almost devoid of lymphoid tissues and is tolerant to homografts. Tolerance represents a specific failure of the immunologic response mechanism and, it may be, development of the ability to destroy antigenic material. Injection into mice, on the day of birth, of 5 to 10 times 10^6 lymphoid cells causes 100 percent of the mice to show a transient tolerance re-

sponse and 80 percent to keep homologous grafts for at least 100 days.

Morgan Harris discussed the selected uptake and release of substances by cells. He showed that the passage of proteins into cells can be demonstrated with fluorescent antibodies. Phagocytosis or pinocytosis are possible mechanisms for the movement of protein into cells; the uptake is of the size of globules. In tissue culture the amount of protein formed in cells cannot be accounted for by the decrease in amount of amino acids. After several days, more than half the cell protein can be shown to come from the protein of the medium. Protein fractions from spleen, liver, and brain are active in promoting the growth of tissue cultures. The spleen is somewhat more active than the others. The protein fraction is effective without the nucleic acid. It is suggested that the nucleic acid of nucleoproteins may act as a stabilizing factor, for freezing and thawing destroy the protein activity but not the nucleoprotein activity. Lactic acid production by tissue culture showed that the addition of heterologous serum caused an increase in glycolytic rate. Glycolytic rate was defined as the rate of production of lactic acid. On the other hand, embryo extract produces a lower glycolytic rate. Greater formation of lactic acid can be shown in muscle cell cultures than is reported for tumor tissues by Warburg and by Burk and others. In the discussion of this paper it was brought out that protein is not used by cultures of HeLa cells, that the lactic acid formation by tissue culture is a function of the substrate rather than a function of the metabolism of the cell, and that it is impossible to compare lactic acid formation by one type of cell with that by another unless the same substrates have been used.

N. T. Spratt studied control mechanisms in development and demonstrated several factors controlling chemically the growth of cells. In tissue cultures, the smaller the population of cells, the poorer the resistance of the cell population to changes in the environment. This was shown to be the result of the requirement for carbon dioxide. The more cells there were present, the more carbon dioxide was formed, producing a more favorable environment for all the cells. The effect of various sugars showed that there was a differential in the need for carbohydrates in various areas of the embryo. The chick embryo thrives best on a medium containing glucose or mannose. Maltose, fructose, and galactose will each support more or less growth, in decreasing order. Each of these is less effective than glucose. Pyruvate and lactate are very poor supporters of development, particularly of neural tissue. As the concentration of carbon available is lowered, the brain is first affected. The most active cells appeared to be most affected by alterations in the substrate. Alterations in ions show that with diminution of potassium in the medium there is fairly normal growth of most tissues but essentially no development of the heart. Oxygen removal causes serious changes in the most active centers of the embryo. A condition of anaerobiosis and the presence of malonate and cyanide permit development of the heart but of no other organ. Fluoride prevents development of the heart, but the brain is not affected. The effect of fluoride can be reversed by pyruvate. Iodoacetate inhibits development of the brain and the central portion of the embryo, and this effect is reversed by pyruvate. It seems as if the changes of embryogenesis are much too subtle to be simple effects of carbon dioxide, carbon source, oxygen supply, and so on. Surviving liver and heart slices and homogenates inhibit the development of embryonic tissues when there is intimate contact between the embryo and the tissue. Heating the tissue or taking it out of contact with the embryo keeps it from having this effect. The following functions, in ascending order, parallel the increase in carbon source: maintenance, movement, differentiation, and growth. In general, as a nutritive source, carbohydrate is less effective than amino acid, which is less effective than protein in the form of albumin, which is less effective than yolk protein.

Rita Levi-Montalcini, in the study of the chemical stimulation of nerve growth, showed that extracts of sarcoma stimulated the growth of sensory and sympathetic nerve tissue but not motor nerve tissue. This could be demonstrated in increase in cell activity, in mitosis, and in the speed of differentiation of cells. It could be shown that this soluble material stimulates the growth of nerve cells in tissue culture. Snake venom and extracts of salivary gland of the mouse were seen to have the same effect. S. Cohen studied the nature of this stimulating agent and found that it was active in tissue cultures at a concentration, for tumor extract, of 15 mg/ml; for snake venom, of 6.5 μg/ml; and for submaxillary gland extract, of 1.5 μg/ml. Neurotoxic snake venom showed no greater activity than other kinds of snake venom. A purification of the factor showed that it was a protein, stable in 0.1*M* alkali. Its molecular weight by sedimentation was approximately 20,000. It was not found to have the activity of any of the known enzymes of snake venom. Although its activity is inhibited by antisera to snake venom, the activity of the protein obtained from salivary gland is not inhibited by antibody to snake venom. In a study of the formation of nerve fibers by tissue-cultured cells under the influence of the nerve-growth factor, it was found that indoacetate could inhibit this growth but that cyanide, fluoride, and dinitrophenol could not. Glucose or mannose are needed for growth of the fibers. Phenylalanine is also needed. This was shown indirectly because there is apparently enough amino acid in the tissues to prevent a nutrition experiment from being performed. But parafluorophenylalanine will inhibit the growth of fibers.

Leslie Foulds described the developmental aspects of carcinogenesis. Observation of the development of breast tumors in mice revealed the fact that tumors would grow with each pregnancy and would regress at parturition. In mice bearing several tumors this cycle could be repeated many times. Finally, one of the tumors would fail to regress following pregnancy and would continue to grow at the same rate as previously. This tumor, however, would be malignant and could be histologically demonstrated to be so. The tumor which becomes malignant is not necessarily the first one that appeared. The histologic type of the tumors which appeared and regressed was markedly different from the histologic type of the tumor which appeared and continued to grow beyond parturition. At times, two or more of these new tumors would grow within the "plaques" of tumors which regressed with parturition. The small islands of potentially malignant cells lying within the subcutaneous tissues were discussed in relation to their similarity to the islands of malignancy which developed within the "plaques" in the mammary tumors.

Elio Borghese discussed the growth of organs in tissue culture. He showed the effect of induction of organ structure across distances which prevented contact of cell processes. An interesting effect of insulin—shortening of the shafts of bones, and epiphyses—was demonstrated.

Derst Hadorn, in studies of fruit flies, investigated the role of genes in the developmental processes. The suggestion was made that the further the process of ontogenesis has advanced, the more genes are necessary for growth. Certain genes are apparently essential for particular phases of development. An experiment was reported in which the relation between uric acid metabolism and the eye pigment isoxanthopterin was established. It was found that xanthine oxidase is missing from the *Drosophila* mutant "rosy." Xanthine oxidase is necessary for the oxidation of both xanthine and hypoxanthine as well as for the oxidation of the precursor of isoxanthopterin. Therefore, it was noted that the step-wise insertion of characteristics of gene action is not necessarily related to the apparent action of the gene, for the precursor of isoxanthopterin is not found in the animal till long after xanthine oxidase appears. Other lethal mutants

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have been demonstrated which cannot synthesize protein from hydrolyzed protein. These protein mutant effects can be demonstrated by analysis of the hemolymph.

Carroll Williams discussed the hormonal regulation of metamorphosis. Experiments with the pupation of the moth suggest that specific cells appear to be programmed for various stages through which the organism develops and that certain hormonal stimuli accelerate or induce the growth of the organism along these programmed paths. As an example, cuticle formation by the epidermal layer was cited, as well as experimental evidence developed on the basis of the movement of areas of color, hairiness, and intersegmental membranes. The prothoracic gland apparently controls the conversion of pupa to adult. The hormone isolated from the prothoracic gland of the silkworm by Karlson and Butenandt has been named by them "ecdyson." This appears to be the growth hormone for all arthropods, which comprise more than 90 percent of the animal kingdom. Ecdyson, alone, stimulates both growth and differentiation of all tissue except muscle. Growth and differentiation of muscle requires a neurohormone apparently secreted by neurosecretory cells in the brain. Both the medial and lateral neurosecretory cells of the brain are needed to produce brain hormones. Pilocarpine can block the neurosecretory effect. This has been shown to be due to the imidazole ring structure. The brain hormone is a trophic hormone for the prothoracic gland. The diapause begins when the brain "shuts off." "Low temperature" starts the brain again. Therefore, the brain appears to be itself subject to neuronal stimuli. The slowing down of differentiation is due to another hormone called the "juvenile hormone," found in the corpora allata. The hormone of the corpora allata has been concentrated and seems to be a steroid. Beef adrenal cortical extract has the capacity to do the same thing as the juvenile hormone, but none of the known steroids has been identified as the juvenile hormone.

A report by André Glinos on the mechanism of liver growth and regeneration demonstrates that in normal serum there is an inhibitor to the mitotic activity of the liver. This inhibitor has been related to the albumin concentration of the serum. Even a small increase in the albumin content of the extracellular fluid of the liver inhibits the formation of albumin by liver cells and actual growth of liver tissue as determined by mitotic counts. On the other hand, diminution of albumin content of the extracellular fluid stimulates growth, mitosis, and albumin formation by the liver cells. This feedback mechanism is concerned solely with albumin synthesis and growth. Since albumin synthesis occurs only in the liver, there is no relation of this effect to the growth of any other tissues.

A detailed report of the proceedings of this symposium, edited by McElroy and Glass, will be published by the Johns Hopkins Press.

SAMUEL P. BESSMAN
School of Medicine,
University of Maryland, Baltimore

Weak Interactions

The American Physical Society and the Oak Ridge National Laboratory are sponsoring a Conference on Weak Interactions to be held in Gatlinburg, Tenn., 27–29 October. Although as planned the specialty of the conference will be β-decay, it will also be concerned with π- and μ-decay, as well as strange particle decay. There will be invited speakers at each session to review the subject for the session. Each session will also have contributed papers.

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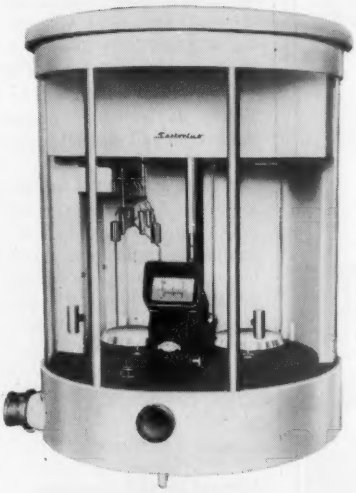

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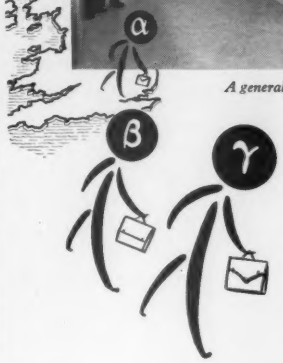
A general view of one of the isotope laboratories.



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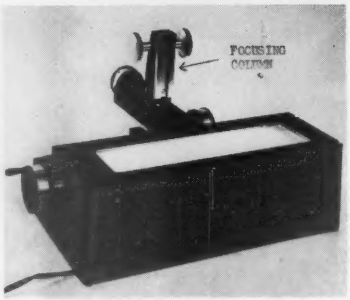

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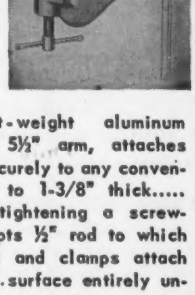

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should be sent to J. L. Fowler, Oak Ridge National Laboratory; the deadline date is *24 September*. These summaries may be, but do not necessarily have to be, somewhat longer than the 200-word abstract customarily used by the Physical Society, and may also include a few figures somewhat in the style of Letters to the Editor. They should not, however, exceed 600 words in length. Standard 200-word abstracts should also be submitted, for these will be published in the *Bulletin* of the American Physical Society.

Medicine and Biology

The eleventh annual Conference of Electrical Techniques in Medicine and Biology will be held in the Nicollet Hotel, Minneapolis, Minn., 19–21 November, under the sponsorship of the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the Instrument Society of America. The meeting will be chiefly devoted to the use of computers in medicine and biology.

One special session will be on the possibility of applying computers to the theoretical and clinical problems of electrocardiography. Another session will deal with computers in electroencephalography. A third special session will be on the inverse problem of developing computer application on the basis of biological coding, biological transducer designs, and biological logic. The meeting is open to all scientists, engineers, and physicians. Abstracts, 250 words, should be sent before *1 October* to Mr. Robert Erskine, Minneapolis–Honeywell, 2753 4th Ave. S., Minneapolis, Minn.

Mental Health Seminars

"Implications for Psychiatry of Recent Researches on Animal Behavior" will be the general topic of the second International Seminars on Mental Health to be presented in October by the Post-graduate Center for Psychotherapy. Konrad Z. Lorenz, director of the Max Planck Institute of Westphalia, Germany, will address a series of conferences on his recent findings in the field of ethology which will help throw new light on man's behavior.

Lorenz's schedule follows: 10 October, evening panel discussion, "Social Aggression and its Inhibition in Animals: Implications for Psychoanalytic Theory," New York Academy of Medicine; 12–15 October, Josiah Macy, Jr. Foundation conference, Princeton, N.J.; 16 October, research seminar, Yale University School of Medicine, New Haven, Conn.; 20 October, 1958–59 Downey seminars on "Modern Concepts in Psychiatry," Veterans Administration Hospital, Downey,

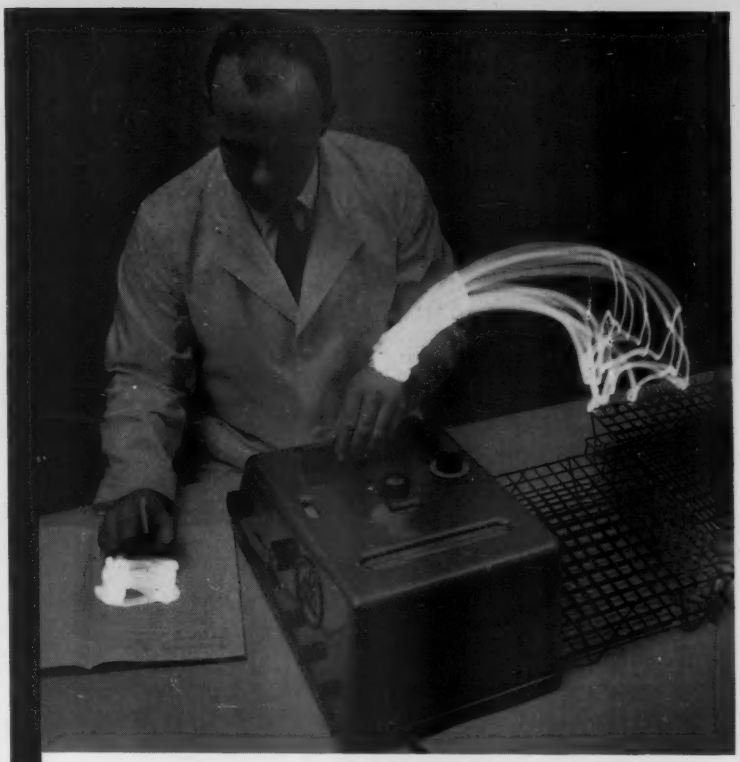
Ill., Northwestern University Medical School VA Training Program; 21–24 October, Menninger Foundation, Topeka, Kan. (including Menninger Forum, 22 October); 26 October, all-day conference (by invitation only), "Unlearned Communicative Processes Between Animals: Implications for Bio-social Adaptation Theory," Postgraduate Center for Psychotherapy, New York; 30 October, evening panel discussion, "Physiological and Psychological Aspects of Unlearned Motor Patterns: Afferent Control, Spontaneity and Relations to Learning," American Museum of Natural History (cosponsor), New York.

The Postgraduate Center for Psychotherapy has established the International Seminars on Mental Health to present at the Postgraduate Center and throughout the United States distinguished scientists from abroad to introduce new ideas and approaches that may be integrated into American psychiatric theory and practice. The seminars, which are sponsored by the World Federation for Mental Health, are underwritten by a grant from the Samuel Rubin Foundation.

Air Pollution

At a meeting in Washington in August a group of specialists in air pollution control met with Public Health Service officials to discuss plans for the first national conference on air pollution to be held 18–20 November at the Sheraton Park Hotel, Washington, D.C. The plans call for plenary sessions—with addresses by scientists, industrialists, and government officials—and group meetings in which recommendations will be formulated for future action. Subjects to be considered will include effects of air pollution on health, control methods, economic factors, and so forth.

The planning group that met in Washington included the chairmen and co-chairmen of six discussion panels: Arie J. Haagen-Smit, Division of Biology, California Institute of Technology, and H. C. McKee, Southwest Research Institute, San Antonio, Tex.; S. L. Hanauer, Department of Air Pollution Control, City of New York, and Leslie Chambers, Los Angeles County Air Pollution Control District; John T. Middleton, Citrus Experiment Station, University of California, and Arthur Crago, American Cyanamid, Brewster, Fla.; Malcolm H. Merrill, California Department of Public Health, and James P. Dixon, Commissioner of the City of Philadelphia; Leslie Silverman, Harvard University School of Public Health, and W. C. L. Hemeon, Hemeon Associates, Pittsburgh, Pa.; Louis C. McCabe, Resources Research, Inc., Washington, D.C., and Harold W. Kennedy, County Counsel of Los Angeles.



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Forthcoming Events

October

12–17. American Acad. of Ophthalmology and Otolaryngology, Chicago, Ill. (W. L. Benedict, 100 First Ave. Bldg., Rochester, Minn.)

13–15. Association of American Medical Colleges, 69th annual, Philadelphia, Pa. (W. Darley, AAMC, 2530 Ridge Ave., Evanston, Ill.)

13–15. National Electronics Conf., Chicago, Ill. (L. W. Von Tersch, Michigan State Univ., East Lansing.)

13–16. Society of Exploration Geophysicists, 28th annual intern., San Antonio, Tex. (C. C. Campbell, Box 1536, Tulsa 1, Okla.)

13–17. American Soc. of Civil Engineers, annual conv., New York, N.Y. (W. H. Wisely, ASCE, 33 West 39 St., New York 18.)

14–15. National Acad. of Economics and Political Science, fall annual, Washington, D.C. (D. P. Ray, George Washington Univ., Washington 6.)

15–17. American Ceramics Soc., Glass Div., Bedford, Pa. (C. S. Pearce, 4055 N. High St., Columbus 14, Ohio.)

19–22. Land and Water, Soil Conservation Soc. of America, 13th annual, Asheville, N.C. (H. W. Pritchard, 838 Fifth Ave., Des Moines 14, Iowa.)

19–24. American Soc. of Anesthesiologists, Pittsburgh, Pa. (J. E. Remlinger, 802 Ashland Ave., Wilmette, Ill.)

19–26. Allergology, 3rd intern. cong., Paris, France. (S. M. Feinberg, Medical School, Ward Memorial Building, 303 East Chicago Ave., Chicago, Ill.)

19–26. Medical Hydrology, 21st intern. cong., Madrid, Spain. (Dr. Francon, 55, rue des Mathurins, Paris 8e, France.)

20–21. Rubber and Plastics Instrumentation, natl. symp., Akron, Ohio. (D. R. Davis, General Tire and Rubber Co., Central Research Lab., Akron 9.)

20–22. American Oil Chemists' Soc., fall, Chicago, Ill. (Mrs. L. R. Hawkins, 35 E. Wacker Drive, Chicago 1.)

20–23. American Acad. of Pediatrics. Chicago, Ill. (E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill.)

20–23. American Psychiatric Assoc., Kansas City, Mo. (1700 18 St., NW, Washington 6.)

21. American Soc. of Safety Engineers, annual, Chicago, Ill. (J. B. Johnson, 425 N. Michigan Ave., Chicago 11.)

22–24. American Assoc. of Petroleum Geologists, southwestern, Mineral Wells, Tex. (R. H. Dott, Box 979, Tulsa 1, Okla.)

22–24. Aviation Medicine, 4th annual symp., Santa Monica, Calif. (T. H. Sternberg, UCLA Medical Center, Los Angeles 24, Calif.)

22–26. American Soc. for the Study of Arteriosclerosis, annual, San Francisco, Calif. (O. J. Pollak, P.O. Box 228, Dover, Del.)

23–25. National Soc. of Professional Engineers, San Francisco, Calif. (K. E. Trombley, NSPE, 2029 K St., NE, Washington 6.)

23–25. Rocket Technology and Astronautics, intern., Essen, Germany. (Deutsche Gesellschaft fuer Raketentechnik und Raunfahrt, e.v., Neunsteinerstrasse 19, Stuttgart, Zuffenhausen.)

24–25. International Conference on the Insulin Treatment in Psychiatry, New York, N.Y. (M. Rinkel, 479 Commonwealth Ave., Boston 15, Mass.)

24–25. Taxonomic Consequences of Man's Activities, symp., Mexico, D.F. (H. C. Cutler, Missouri Botanical Garden, St. Louis.)

24–28. American Heart Assoc., San Francisco, Calif. (J. D. Brundage, 44 E. 23 St., New York 10.)

27–28. Child Research in Psychopharmacology, conf., Washington, D.C. (S. Fisher, Psychopharmacology Service Center, Natl. Inst. of Mental Health, Bethesda 14, Md.)

27–28. Plant Physiology, 9th annual research cong., Saskatoon, Saskatchewan, Canada. (D. T. Coupland, Plant Ecology College of Agriculture, Univ. of Saskatchewan, Saskatoon.)

27–29. Radio, Institute of Radio Engineers, fall meeting, Rochester, N.Y. (V. M. Graham. EIA, 11 W. 42 St., N.Y.)

27–29. Weak Interactions, APS conf. (by invitation), Gatlinburg, Tenn. (J. L. Fowler, ORNL, P.O. Box X, Oak Ridge, Tenn.)

27–31. American Inst. of Electrical Engineers, fall general, Pittsburgh, Pa. (N. S. Hibshman, AIEE, 33 W. 39 St., New York 18.)

27–31. American Public Health Assoc., St. Louis, Mo. (B. F. Mattison, 1790 Broadway, New York 19.)

(*See issue of 15 August for comprehensive list*)

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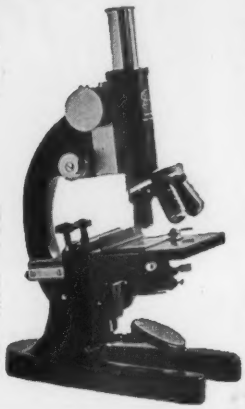

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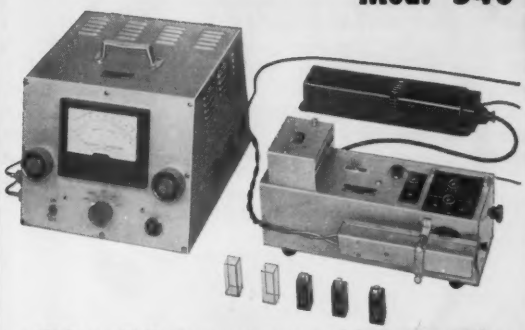

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Letters

Lepeshinskaia

Readers of *Science* will be interested to learn that Lepeshinskaia, whose work was reviewed recently there (*1*), has been pressing her "anti-Virchowian thesis" since the early thirties. This thesis states that cells continuously originate from "undifferentiated organic matter"in such a way that living matter recapitulates, in ontogenesis, not only its phylogenetic cellular past but also the precellular phases of biochemical development which, eons ago, presumably led to the first appearance of living entities on earth. Her colleagues refused to take her seriously for the longest time. In the beginning, if they deigned to notice her at all, it was only to point out elementary defects in her laboratory technique and the like (*2*). How she managed not only to survive the contempt of her colleagues but to advance in spite of this to receive the official accolade in 1950 on behalf of her "dialectical materialist theory of cellular development from undifferentiated organic matter" is a story that still awaits telling.

Lepeshinskaia has also been interested in the aging process and has advanced the notion that a 1-percent soda solution slows aging and has healing properties. She likewise believes that the solution increases harvest yields (*3*)! However, little of late has been heard of these extravagant claims. It should be noted that, although her theories were proclaimed as official, their effect has not been particularly baleful, in that *de facto* resistance to them has been in continuous evidence. Mindful of the genetics tragedy in the Soviet Union, one can easily exaggerate the harm wrought by Lepeshinskaia. But she was no Lysenko (*4*).

IVAN D. LONDON

Brooklyn College, Brooklyn, New York

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1. L. N. Zhinkin and V. P. Mikhailov, *Science* 128, 182 (1958).
2. N. K. Kol'tsov, *Biol. Zhur.* 3, 255 (1934); B. Tokin, *Pod Znam. Marksizma* 16, 116 (1936).
3. O. B. Lepeshinskaia, *On Life, Age, and Longevity* (Znanie, Moscow, 1953).
4. I. D. London, *Bull. Atomic Scientists* 13, 169 (1957).

Author Listings in References

References to previous work in scientific reports facilitate the weaving of new facts into the fabric of our knowledge. Authors' names are an essential part of such references.

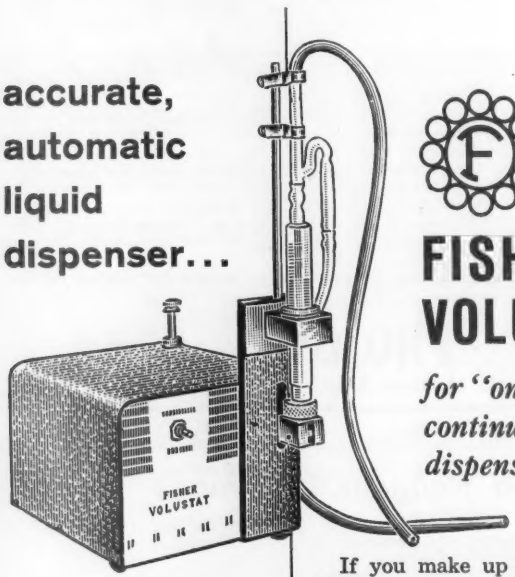
Science prints names of authors of quoted articles if there are three or less in number but uses the first author's name and *"et al."* when there are more than three authors. This is a disservice to those interested in such articles. Author names in references are omitted in the text by some journals, often a questionable practice. Even in such instances all the authors are listed in the bibliography. To list all the authors neither in the text nor in the bibliography, as in *Science,* leaves the reference incomplete. It also prevents best integration of the new information.

These are days of extensive cooperative and interdisciplinary research, with several workers attacking problems and publishing the results jointly. The choice of a senior author is often dictated only by the fact that one name, of necessity, must be first, and by no other consideration. Surely the printing of complete references by listing all authors will not put an undue burden on *Science,* which is otherwise so generous with space in its fine new typographical make-up.

Z. I. KERTESZ

New York State Agricultural Experiment Station, Cornell University, Geneva, New York

Done—THE EDITORS.



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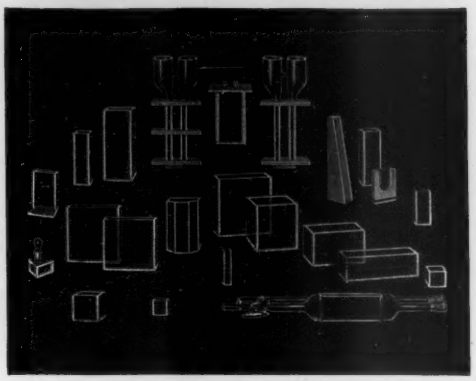

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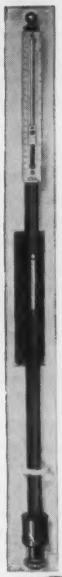

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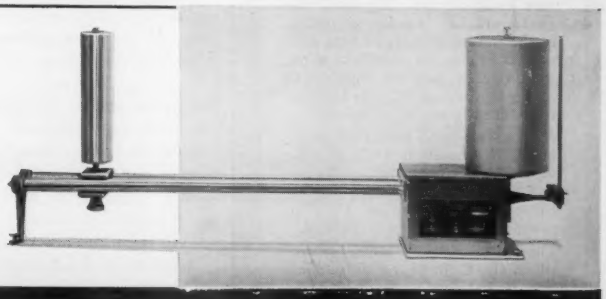

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■ FREQUENCY-TO-VOLTAGE CONVERTER can be adjusted in a full-scale frequency range from 300 to 900 cy/sec, with a minimum frequency of 10 cy/sec. Output may be 0 to 5 v, 0 to 100 mv, or 0 to 50 mv, d-c. Linearity is ±0.1 percent of full scale. Long-term stability is ±0.25-percent. The device will operate in ambient temperatures from −65° to +160°F. (Fischer & Porter Co., Dept. 314)

■ FRACTION COLLECTOR accessory for a gas chromatograph consists of a chromatograph column, with a sample range up to 5 ml, and the collection apparatus. Fractions eluted from the column are condensed in fluted glass collection tubes inside a Dewar flask. Fractions are compacted by centrifugation. (Beckman Instruments Inc., Dept. 315)

■ Q COMPARATOR provides comparison measurements of relative Q, inductance, and capacitance. The instrument is set up for use with a standard component. Other components are compared with the standard by connection into the test circuit and by observation of the displacement of a centered spot in a cathode-ray-tube display. Deviation along the vertical axis indicates a change in Q and deviation along the horizontal axis indicates a change in L or C. (Boonton Radio Corp., Dept. 316)

■ COLORIMETRIC TITRATOR combines a photoelectric colorimeter with a titration adapter to permit objective determination of end-point. The adapter is self-contained and includes a stirring motor and stirrer. A glass cuvette of 35-mm light path serves as a titration vessel. Modification of the colorimeter is not required for installation of the adapter. (Photovolt Corp., Dept. 317)

■ TEMPERATURE TEST CHAMBERS are designed for compatibility with hydraulic or electrodynamic vibration generators. The chambers are mounted on castered legs. An aperture in the bottom of the chamber permits mounting of a stand-

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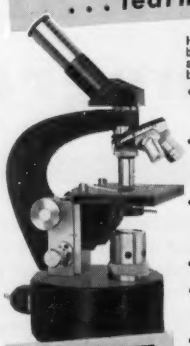

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off by which test specimens may be connected to the vibrator. Heating is electrical; cooling uses solid or liquid CO_2 or mechanical refrigeration. Various sizes and ranges are available. (Wyle Associates, Dept. 319)

■ VACUUM DESICCATOR of transparent plastic is spherical in shape. The working height at the center above a 9¼-in. diameter porcelain plate is 6½ in. Weight is said to be 52 percent less than glass and 57-percent less than aluminum. (Ace Glass Inc., Dept. 320)

■ MERCURY ARC LAMP is a water-cooled type available in models rated at 900-w input and 60,000-lu output, or 1 kw and 65,000 lu. Arc dimensions are 2 by 25 mm. The average life for continuous operation is 80 hr. Operation may be on a-c, d-c, pulse, or stroboscopic power. (PEK Labs, Dept. 321)

■ TEMPERATURE INDICATORS for use with resistance thermometers are battery operated. Standard range is 0° to 500°F. Single and multichannel instruments are available. Temperature is indicated directly. Scale divisions are 10°F and 10°C, and controls permit calibration to ±20°F. (Arthur C. Ruge Associates, Inc., Dept. 322)

■ ELECTRONIC COUNTER provides an eight-decade indication and frequency range from 10 cy to 10 Mcy/sec. Time intervals from 1 μsec to 100 days can be measured. Magnetic beam-switching tubes are used for counting, numeral-electrode indicator tubes for display. Frequency-converter units, video amplifiers, extended time-base units, relay test units, and digital recorders are available as accessories. (Lavoie Laboratories, Inc., Dept. 323)

■ MULTIPLEXER provides means to couple five separate voltage inputs to a single voltage output. The devices are of modular design and are interconnectable. For example, four units would provide for time multiplexing of 20 channels to one output. Maximum sampling rate is 25 kcy/sec. Standard input range is ± 10 v, but other ranges from ± 2 to ± 300 can be supplied. Transfer accuracy is ± 0.05 percent of full scale. (Epsco, Inc., Dept. 324)

■ MICROMETER KIT for use with the manufacturer's series 280 metering valves permits measurement of valve settings required to obtain a desired flow. All parts necessary for installation, as well as instructions, are furnished. (Hoke, Inc., Dept. 326)

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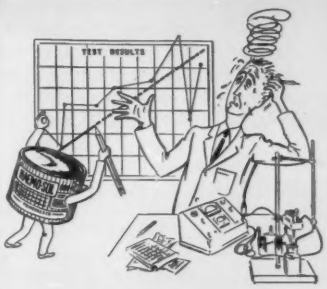

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■ SENSITOMETER for testing of photosensitive materials is essentially a contact printer with an electronic xenon-filled flash tube as the exposing light. Three capacitor circuits provide exposure times of 1/100, 1/1000, and 1/10,000 sec, selected by a pushbutton. A standard step negative is printed to make the measurement. Filters permit change of the light-source color from daylight to incandescent. (Edgerton, Germeshausen & Grier, Inc., Dept. 327)

■ OPTICAL PROJECTOR for inspection of contours makes it possible to inspect objects covering a field of 6 in. at a magnification of 10. The instrument's transparent screen is 60 in. wide by 40 in. high. (Optical Gaging Products, Inc., Dept. 328)

■ LIQUID-NITROGEN GENERATOR, a self-contained unit, is fully automatic in operation, producing pure liquid nitrogen from atmospheric air. Production rate is approximately 4 qt/hr. Floor space required is 20 by 72 in. (Philips Electronics Inc., Dept. 334)

■ MINIATURE SYRINGE permits direct reading of fractions of a microliter. The smallest model has a capacity of 10 μl and a dead volume of 0.5 μl. The needle is 0.018 in. in diameter and 2 in. long. (Hamilton Co., Dept. 335)

■ GLOSSMETER measures 20°, 60°, and 85° ASTM gloss of materials. Gloss readings are indicated on a 7.5-in. meter. A single standard suffices for calibration of complete ranges at all angles. Standardization can be accomplished in 30 sec. Substitute aperture plates permit estimation of the sharpness of source image. (Manufacturers Engineering & Equipment Co., Dept. 337)

■ GAGING HEAD features a constant measuring pressure and has graduations of 20 μin. and a dial range of ± 0.001 in. Measuring accuracy is stated to be ± 10 μin. over the entire range. The sapphire-tipped contact point is lifted and lowered by a cable release to avoid effects of heat from the operator's hand. Instrument size is 2½ by 3¾ in. (George Scherr Co., Dept. 339)

■ RATIO COMPUTER accepts two independent d-c signals as low as 1-mv full-scale per channel and computes their ratio with ± 1-percent accuracy. The computer contains two d-c differential chopper preamplifiers, a power supply, and a servo divider. Response time is 1 sec. (Magnetic Instruments Co., Dept. 338)

■ WARBURG APPARATUS is a bench model designed for use where space is limited; diameter is 16 in., weight 63 lb. Four pairs of operating manometers and one thermobarometer are accommodated. Rotation of the manometer table is unlimited in either direction. Temperature range is ambient to 50°C. (American Instrument Co., Inc., Dept. 336)

■ VACUUM-TUBE VOLTMETER for a-c uses a vacuum thermocouple as its detector. Measurements are made by comparing the unknown voltage with an accurately calibrated 1000-cy/sec signal. Accuracy is ± 0.5 percent from 50 cy to 5 kcy/sec, and ± 2 percent from 10 cy to 500 kcy/sec. Voltage range is 300 μv to 1 kv. (Millivac Instruments, Dept. 318)

■ ULTRASONIC CLEANERS are available in ⅛- and ⅜-gal capacity. Ultrasonic generators are furnished with or without timers. Power output to transducers is 35 w (average), and 140 w (pulse) at 90 kcy/sec. The cleaners operate on 115 v, 60-cy/sec power. They weigh 10 lb. (Narda Ultrasonics Corp., Dept. 343)

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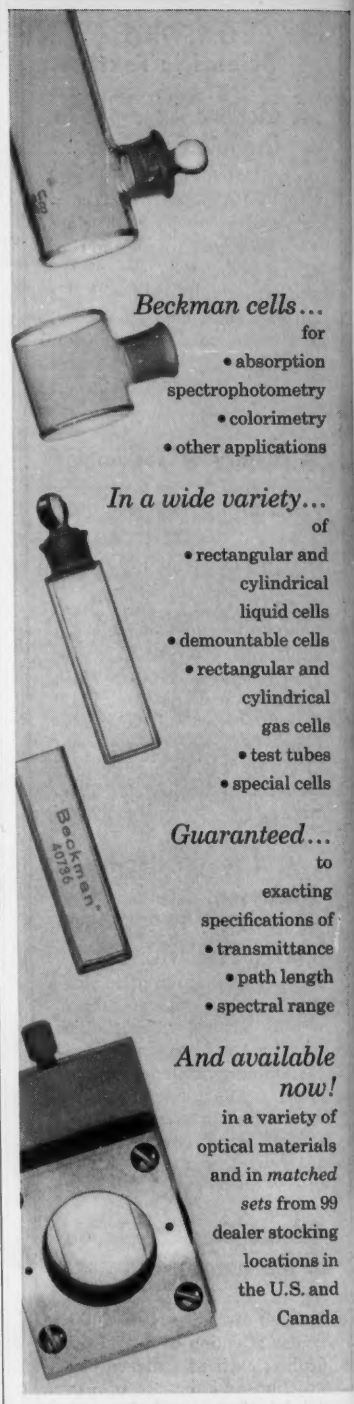

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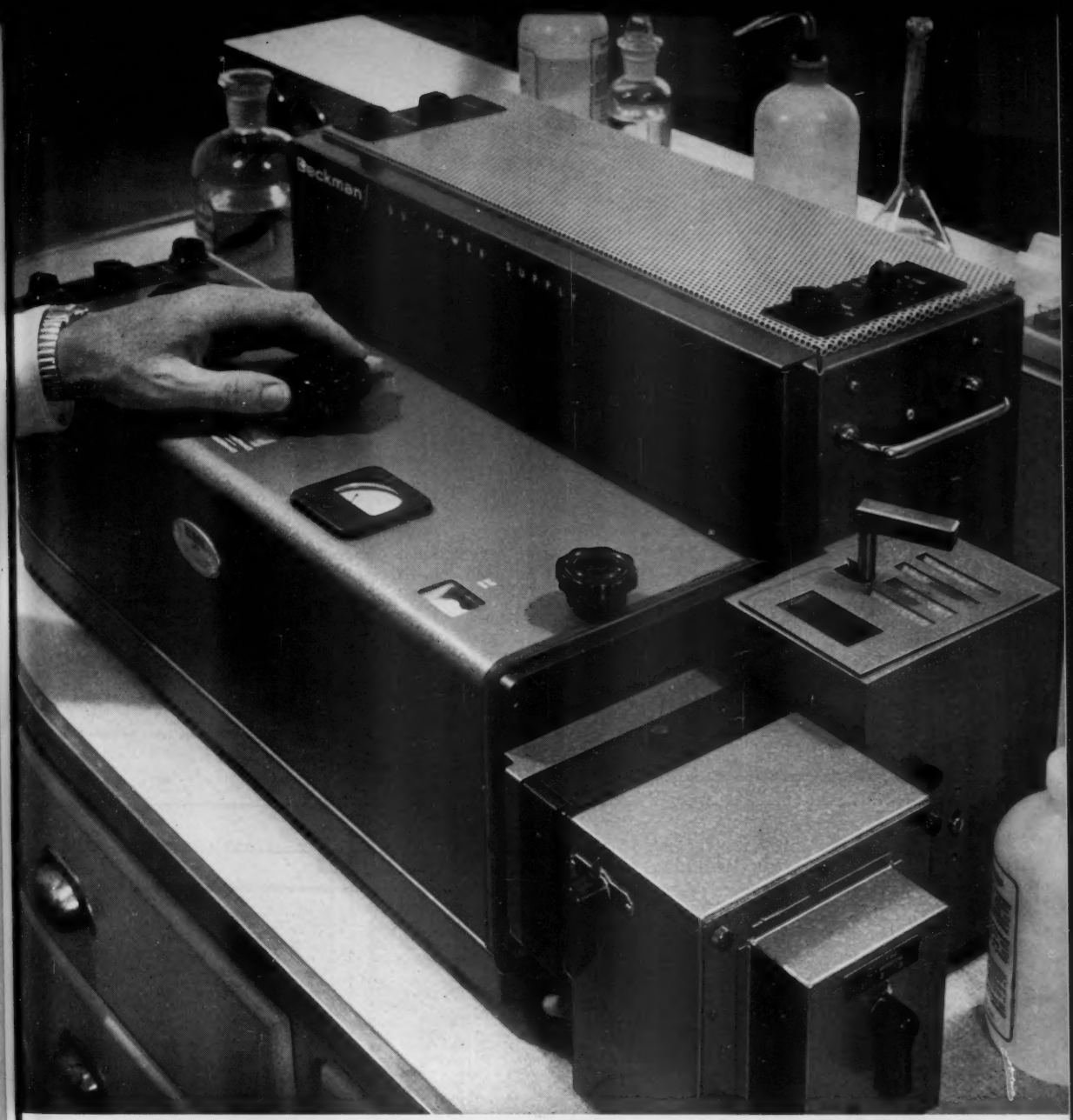

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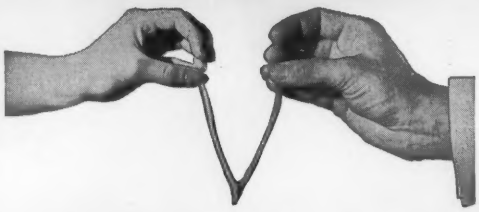

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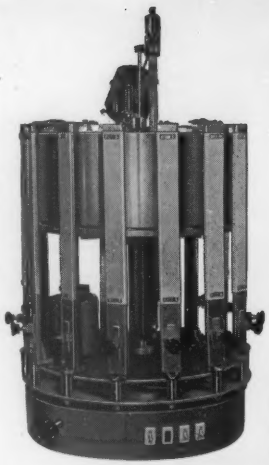

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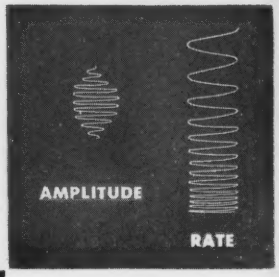

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12 September 1958

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EQUIPMENT

Circle below desired number corresponding to:

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In list below, check page number of advertiser from whom you would like more information. If more than one item appears in ad, letters (A, B, C) are used to indicate particular items available in order of appearance in advertisement. Where more than one ad appears on page, **"U" indicates upper ad, "L" lower ad, "I" inside ad, "M" middle ad,** and **"O" outside ad.** Advertisements in Personnel Placement and Market Place are not keyed. A multiplicity of items is indicated by *. Readers are requested to specify on this coupon the particular item in which they are interested; otherwise, the request cannot be processed.

☐ 558*	☐ 559, A	☐ 559, B	☐ 559, C	☐ 560*
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☐ 606, U	☐ 606, LO	☐ 606, LI	☐ 607	☐ 608
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☐ 616, UO	☐ 619*	☐ 620		

☑ Check the many ways ANTON can serve your nuclear needs

☐ **Anton's Electrically Compensated Ion Chambers and BF_3 Counter Tubes**

(Enriched, normal or depleted in B^{10}) for detection of either slow or fast neutrons are widely-used in reactor control and monitoring, oil well logging and neutron survey. Available in a wide range of diameters, sensitive lengths and wall thicknesses in 2S aluminum or stainless steel.

☐ **Anton End Mica Window Counters**

Alpha, beta, gamma counters are halogen quenched, stainless steel. Also available with special organic as well as other rare gas fills. Window thicknesses available from 1 mg/cm². Tubes vary from subminiature to standard conventional sizes and are based with standard RMA connectors. JAN types available.

☐ **Anton Thin Wall Counter Tubes**

Stainless steel, halogen quenched counter tubes for beta, gamma studies are extremely sensitive and can meet all JAN-MIL specifications. They are the only commercial metal thin wall tubes available with a stainless steel 30 mg/cm² wall which will not dent or collapse. Instruments using groups of these tubes exceed in sensitivity and stability most scintillation units.

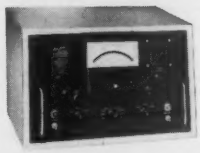
☐ **Anton's Pancake Tubes**

Halogen quenched, sensitive beta-gamma detectors with end mica window. These units are designed for low intensity measurement and are widely used in facilities doing low-count work. Flat pancake design offers advantage of large diameter window without large volume and high background count.

Anton high efficiency tubes are Platinized*. This process provides sensitivity beyond that of standard tubes.

*Reg. pending

☐ **229 Ratemeters**



The most precise laboratory ratemeter available, Anton's 229 Series has 7 scales, including a single log scale from 300-50,000 cpm with accuracy of better than ±2% of meter reading above ⅓ scale. It has dual range input sensitivity and provides precise and efficient measurement of radioactivity in industry, research and medicine.

☐ **700 Survey Meter**

Portable laboratory or field survey meter (.5; 5; 50 mr/hr full scale) is built to FCDA specifications – the only CDV-700 type survey meter which can be exposed continuously to high intensity radiation without detector failure. Probe uses Anton halogen quenched, very thin wall, stainless steel counter tube. Accuracy assured from −55°C to +75°C.

☐ **44 Ratemeter**

Low-cost, accurate, dual range (0-5000; 0-50,000 cpm) . . . exclusive input design. Supplied with Anton long-lived, stainless steel, halogen quenched, thin wall (30 mg/cm²) counter tube or a wide range of other tubes. Unit features a jack for external meters, terminal board construction and oscilloscope connections.

☐ **6001 Sample Changer**

For quick, accurate measurement of low intensity radiation. Designed for use of one or two Anton pancake type, high beta sensitivity, low background counter tubes. Provides 2" lead plus 3/16" aluminum shielding in all directions, lowering the background count by a factor of from two to four. Makes possible counting geometry of nearly 100%.

☐ **High Pressure Reactor Connectors**

Anton's stainless steel, hermetically sealed reactor heater-end connector withstands 2000 PSI at temperatures of 636°F, with terminals capable of carrying a load of 16 amperes with a potential drop of less than 10 milliwatts. A wide variety of conventional and specialized connectors is available.

☐ **Medical Eye, Brain And Ingestion Probes**

These tubes are rugged, sensitive alpha, beta, gamma radiation detectors specifically designed for reliable, low count medical tracer work. They can be cold sterilized and their pulse intensity obviates the need for a preamplifier.

☐ **Air Particle Monitors**

Monitoring systems for aerosol contamination (alpha, beta, gamma) are available in a full range of moving filter paper, fixed filter paper and impact instruments. Rack mounted, cart mounted and portable instruments available.

☐ **Corona Discharge V-R Tubes (300V-30KV)**

Anton is licensed under the basic patents in this field. Valuable data available concerning this low-cost solution to high voltage low current regulation problems.

. . . and many more. **SEND FOR FREE DATA CONCERNING YOUR SPECIFIC NUCLEAR INSTRUMENT, TUBE OR COMPONENT NEEDS.**

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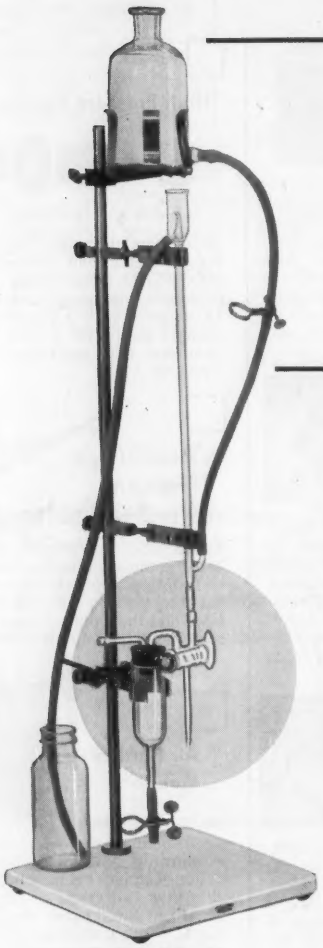

8209-F

Thomas-Seligson
AUTOMATIC PIPETTE*
WITH COMPLETE ASSEMBLY OF ACCESSORY EQUIPMENT

A fixed volume pipette permanently attached to a double bore stopcock, which permits rapid filling without adjustment to a reference mark, and complete washout delivery of the contained sample by a measured amount of a second liquid from a burette, pipette, or arbitrarily calibrated tube connected to upper arm. Eliminates need for individual sampling pipettes, and repeated filling of dilution pipettes, realizing a highly significant economy of time and glassware, and assuring reproducible sampling, delivery, and dilution which are especially important in routine clinical chemistry. Applicable, however, to any type analysis in which a standard volume is diluted or reacted directly with a measured volume of a second liquid. See *American Journal of Clinical Pathology, Vol. 28, No. 2 (Aug., 1957), pp. 200-207.*

In use, the pipette is attached to the dispensing burette by means of the upright arm of the stopcock, and to a suction device by means of the bent tube at the left. A waste trap is inserted into the line prior to the suction connection.

Samples are taken by setting stopcock to connect tip with suction line. A small excess is drawn over into the bent tube to serve as an initial rinse for the pipette wall. The sample is delivered by reversal of the stopcock plug to allow solution in the burette to expel the sample through the tip, and to rinse it clean. Following delivery of the required amount of reagent from the burette, the tip, filled with diluent which keeps it clean, is ready for immediate intake of the next sample.

An assembly of accessory equipment for convenience in making multiple dilutions is offered below. It consists of an automatic zeroing type burette with reservoir for washout of sample and addition of diluent or reagent, trap for suction line, waste receiver, support and necessary clamps and tubing for connections.

...eliminates individual sampling pipettes and repeated filling of dilution pipettes

8209-F. Thomas-Seligson Automatic Pipette Assembly, complete as shown in illustration. Without suction device. With automatic zeroing type Burette 10 ml in 1/20ths. *When ordering, please specify size of Pipette required* **55.35**

8209-B. Pipettes, Seligson, only, as above described.

To contain, ml.....	0.05	0.1	0.2	0.5	1.0
Tolerance, ml (±).....	0.005	0.005	0.01	0.01	0.05
Calibrated stem, mm...	65	55	65	160	140
Each.....	**11.00**	**11.00**	**11.00**	**11.00**	**11.00**

*Patent applied for.

Copy of Bulletin 131 sent upon request.

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